**Standard Operating Procedure for Identifying, Recording and Reporting Adverse Events for Clinical Trials of Investigational Medicinal Products**

**Number:** UM/UoM Pharmacovigilance.Reporting Adverse Events/SOP10(i)/6.0  
**Title:** Standard Operating Procedure for Identifying, Recording and Reporting Adverse Events for Clinical Trials of Investigational Medicinal Products  
**Version:** 6.0 (March 2018)  
**Effective Date:** March 2018  
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**Review Date:** March 2020  
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**Position:** Research Governance, Ethics and Integrity Manager  
**Position:** Chair of Clinical Trials Management Group  
**Signature:**  

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<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Reason for change</th>
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| 2.0     | January 2013| Update of weblinks and office details  
SOP10 (i) has an associate SOP 10 (ii) related to DSURs |
| 3.0     | May 2014    | Addition of version control statement for SOP                                      |
| 4.0     | October 2015| Update of weblinks and office details                                             |
| 5.0     | August 2016 | Updates including eSUSAR weblinks and office details                              |
| 6.0     | March 2018  | Current Process Review and Update                                                 |

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DEFINITIONS

AE Adverse Event (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). Each initial AE will be considered for severity, causality or expectedness and may be reclassified as a serious event or reaction based on prevailing circumstances.

AR Adverse Reaction (any untoward and unintended response in a subject to an IMP which is related to any dose administered to that subject).

CRF Case Report Form or the participant-specific data collection sheet

CTIMP Clinical Trial of an Investigational Medicinal Product

GCP Good Clinical Practice in clinical trials (in accordance with the Medicines for Human Use (Clinical Trials) Regulations (2004 and subsequent amendments)

IMP Investigational Medicinal Product

SAE Serious Adverse Event (an AE that fits the criteria defined as serious in the Regulations – see below)

SAR Serious Adverse Reaction (an AR that fits the criteria defined as serious in the Regulations – see below)

Serious Serious, in relation to an SAE, SAR or SUSAR is an event which either:
a) results in death
b) is life-threatening
c) requires hospitalisation or prolongation of existing hospitalisation
d) results in persistent or significant disability or incapacity, or
e) consists of a congenital anomaly or birth defect.

SUSAR Suspected Unexpected Serious Adverse Reaction (is a SAR that is thought to be ‘unexpected’ i.e. not consistent with the information about the medical product in question set out in the summary of product characteristics (SmPC) or the investigator’s brochure).

UAR Unexpected Adverse Reaction (an adverse reaction the nature and severity of which is not consistent with the information about the medical product in question set out in the summary of product characteristics or the investigator’s brochure.

UoM University of Manchester

1.0 Background

In order to be compliant with the European Directive on Good Clinical Practice in Clinical Trials (2001/20/EC) and The Medicines for Human Use (Clinical Trials) Regulations (2004 and subsequent amendments) organisations conducting Clinical Trials of Investigational Medicinal Products must have clearly documented Standard Operating Procedures covering all aspects of conducting Clinical Trials.

The Regulations set out the legal requirements for pharmacovigilance (adverse event reporting) for clinical trials. To comply with the regulations, those taking on pharmacovigilance...
responsibilities should ensure that the necessary quality standards are in place and are followed for the collection, recording, assessment and reporting of AEs.

A Standard Operating Procedure (SOP) is defined by ICH Harmonised Tripartite Guideline for Good Clinical Practice as “Detailed, written instructions to achieve uniformity of the performance of a specific function”. These SOPs are written instructions and records of procedures agreed and adopted by The UoM.

2.0 Purpose

This SOP applies to all clinical trials that come under the regulations where the University of Manchester has Sponsor responsibility for pharmacovigilance. The requirements of this SOP should be applied as a minimum to such trials. This document describes the responsibilities of both research staff and The University of Manchester (as Sponsor) with respect of the management (identification, recording, reporting and assessment) of AEs, SAEs and SARs which occur within a trial under the regulations. It complies with the principles of GCP for CTIMPs.

In trials where The University of Manchester has entered into a co-sponsorship agreement with a NHS Trust or sub-contracted pharmacovigilance to a clinical trials unit (CTU), i.e. where the delegation log specifies that the NHS Trust/CTU has responsibility for pharmacovigilance, the local Principal Investigator must follow the SOP of the co-sponsor/CTU which has responsibility for pharmacovigilance. The Principal Investigator (PI) has responsibility for notifying all Sponsors of some types of adverse event as per the protocol.

This SOP is designed to be used in conjunction with trial-specific procedures. The AE reporting procedures should be described in the trial protocol and/or trial SOPs. Where an appropriate SOP does not already exist the Chief Investigator (CI) will be required to liaise with the Sponsor to produce one.

3.0 Procedure

3.1 Protocol Development

Before initiating a clinical trial, the CI should give careful consideration to the following:

- The process for collecting, recording, assessing and reporting AEs
- Which AEs should be recorded
- Which AEs should be reported
3.1.1 The process for collecting, recording, assessing and reporting AEs

The proposed procedures for collecting, recording, assessing and reporting AEs should be recorded in the trial protocol and/or trial SOP and will be reviewed by the MHRA during Clinical Trial Authorisation (CTA) assessment.

It is crucial that a clear process for collecting, recording, assessing and reporting AEs is recorded for all trial personnel to follow.

It is recommended that the protocol states that trial participants will be asked at every trial visit whether they have experienced any AEs. The protocol should specify what AE data will be recorded on the trial Case Report Form (CRF) and when a specific AE report form will be used. All AEs should be recorded in the medical notes of the participant.

Once a trial is live the Sponsor will request monthly reporting that will capture this information. In addition, the Sponsor must be provided with all reportable documentation e.g. annual safety reports.

3.1.2 Which AEs should be recorded?

The nature of the AEs to be recorded and reported will depend on the risk assessment of the trial (including the extent of knowledge of the risk profile of the IMP, population to be studied, aims of the trial). Depending on the risks associated with the trial, it may be reasonable to collect one or more of the following:

- All AEs (serious or non-serious) - e.g. where the safety profile of the IMP is not well known;
- Only SAEs – e.g. where the risks and benefits of the IMP is well established;
- Only specific types of SAE – e.g. where the IMP is known to be highly toxic or where the IMP may cause known ARs in a high proportion of participants;
- All ARs (serious or non-serious);
- Only SARs;
- All AEs/ARs of a certain severity (grading using standard toxicity grading scales such as WHO, Common terminology criteria for adverse events (CTCAE)).

In all cases, it should be clearly stated in the trial protocol and/or trial SOP what will be recorded.

3.1.3 Which SAEs should be reported?

CIs are advised to define expected SAEs and SARs in the protocol so that unnecessary expedited reporting can be avoided. For example, in trials where mortality is an end-point, death of a patient from the disease under study can be recorded in the protocol as an expected SAE that does not require immediate reporting. It is strongly recommended that drug reactions that are known to occur with the IMP (i.e. in the Summary of Product Characteristics (SmPC) are listed in the protocol.

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http://www.staffnet.manchester.ac.uk/services/rbess/governance/
Certain trials are undertaken in high morbidity disease where trial primary end-points could also be SUSARs, or when a fatal or other serious outcome is the primary efficacy end-point in a clinical trial. Under these, and similar circumstances, the CI should reach agreement with the MHRA in advance concerning AEs that could be treated as disease related and not subject to systematic unblinding and expedited reporting. Methods of reporting these AEs should be clearly defined in the protocol.

For all CTIMPs and most trials falling under the University's Clinical Trials Management Group, the UoM requires an independent Data Monitoring Committee (IDMC) to be established in order to review safety data on a regular basis (see University SOP14: Data Monitoring Committee and Trial Steering Committee).

Where the University is acting as Sponsor (or Co-Sponsor), and pharmacovigilance has been delegated to a CTU, all SAEs must be reported to the Sponsor using the following email address: saereporting@manchester.ac.uk. The trial name/acronym should be noted in the subject field.

3.2 Identifying Adverse Events and Reactions

3.2.1 The trial protocol should define how AEs and ARs will be identified. For the majority of trials, the local Investigator(s) (or a member of the research team with delegated responsibility to do so) should ask trial subjects at each trial visit about hospitalisations, consultations with other medical practitioners, disability or incapacity or whether any other AEs have occurred since the previous visit. Where the risk assessment dictates, the investigator(s) may be asked to establish a 'hot line' (e.g. email, 24 hour telephone service, etc) in order to expedite the notification of AEs.

3.2.2 AEs may also be identified by support departments, for example, clinical biochemistry, haematology, and radiology. Where notification of such abnormal values or measurements would not occur as standard clinical practice, the procedure for notifying the Investigator (as indicated in the delegation log) of such AEs must be clearly documented in the protocol or trial specific SOPs.

3.3 Recording Adverse Events and Serious Adverse Events

When a research related AE/AR occurs, the local PI should review all documentation (e.g. hospital notes, laboratory and diagnostic reports) relevant to the event. The event and relevant comments should be recorded in the subject’s medical notes (or source data where this is not the medical notes).

3.3.1 The investigator(s) should record all AEs and ARs in detail and file all reports as defined in the trial protocol (usually in the CRF). Those AEs and ARs that are not required to be recorded must be clearly defined in the protocol. This information will provide the basis of the annual safety report required by the MHRA and/or REC as appropriate.
3.3.2 The protocol should state who (usually the investigator(s), or other nominated member or members of the research team) will be responsible for recording and reporting AEs or SAEs. An AE log should also be generated by the party responsible for pharmacovigilance to capture this data and allow signal/trend detection.

The PI should normally be responsible for making an immediate assessment of causality and seriousness. Where a second assessment of an event takes place the causality assessment made by the PI cannot be downgraded. A causality assessment can be upgraded. In the case of a difference of opinion on causality, both assessments are recorded and the “worst case” assessment is used for reporting purposes.

3.3.3 Unless otherwise stated in the protocol, AEs and SAEs should be followed up until resolution or death of the trial subject.

3.4 Assessment of Adverse Events

3.4.1 SAEs must be assessed for seriousness, causality, severity and expectedness.

3.4.2 It is the local Investigator(s)’ responsibility to assess each AE for seriousness and causality. This cannot be delegated to other members of the research team.

3.4.3 Although it is the responsibility of the Sponsor to determine whether a SAR is expected or unexpected. In most cases this responsibility will have been delegated to the CI.

3.4.4 For randomised, double blind studies, AEs should be assessed as though the trial subject was taking the study drug.

3.5 Assessment of Seriousness

An AE should be assessed as serious if it meets one or more of the following criteria:

a) results in death  
b) is life-threatening  
c) requires hospitalisation or prolongation of existing hospitalisation  
d) results in persistent or significant disability or incapacity, or  
e) consists of a congenital anomaly or birth defect.  
f) is medically significant or  
g) requires intervention to prevent any one of the above outcomes.

Medical judgement should be exercised when deciding whether an AE or AR is serious in other situations. The protocol may detail additional criteria which should be classed as serious.
3.6 Assessment of Causality

The local Investigator should make an assessment of causality i.e. the extent to which he or she believes the AE may be related to the study drug. The local Investigator will use clinical judgement to determine the relationship between the IMP and the occurrence of each AE as defined below. Before completing their assessment the local Investigator should consider alternative causes, concomitant therapies, medical history and other risk factors.

Where an event occurs following administration of a drug, the Naranjo Algorithm for Adverse Drug Reaction Causality Assessment (Clin Pharmacol Ther (1981) 30: 239-45) may be used as an aid to interpretation.

**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 to be related**: 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 although the event could have been due to another, equally likely, cause (i.e. the underlying disease, concomitant medication)

**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, it is a known effect of the study drug or its therapeutic class, or based on challenge testing, suggest that the study drug is the most likely cause.

Where an event is classified as possibly, probably or definitely related to the drug it should be recorded as an AR or SAR. Upon learning of an AR or SAR, the CI should review the assignment of causality and discuss this with the local Investigator if (s)he feels necessary.

Where different terms and scales are in use to describe causality between an IMP and an event, this should be specified and explained in the protocol, and the events that qualify as ARs should be made clear.

3.7 Assessment of Severity

3.7.1 The local Investigator should make an assessment of severity for each AR and this should be recorded on the CRF and reported to the Sponsor according to the
following categories:

**Mild**: a reaction that is easily tolerated by the trial subject, causing minimal discomfort and not interfering with everyday activities.

**Moderate**: a reaction that is sufficiently discomforting to interfere with normal everyday activities.

**Severe**: a reaction that prevents normal everyday activities.

3.7.2 The term ‘severe’ used to describe the intensity of an event or reaction should not be confused with the term ‘serious’ which is a regulatory definition based on trial subject/event outcome action criteria. For example, a headache may be severe but not serious, while a minor stroke may be serious but is not severe.

### 3.8 Assessment of Expectedness

3.8.1 If an AR is judged to be related to the study drug, the Sponsor is required to make an assessment of expectedness. However, the University of Manchester, when acting as Sponsor, will usually delegate this to the CI. Whatever the system, it should be agreed and recorded in advance and should be used across the trial. Multi-centre trials should have an arrangement for central review of SAEs to ensure consistency of review.

The expectedness of an AR should be determined according to the reference documents as defined in the study protocol (e.g. the Investigator’s Brochure or the SmPC). It is therefore important to identify all potential ARs in the study protocol.

In summary, ARs may be classed as either:

**Expected**: the AR is consistent with the known toxicity of the study drug and such a reaction is previously identified and described in the study protocol and/or listed in the SmPC or Investigator’s Brochure.

**Unexpected**: the AR is not consistent with the known toxicity of the study drug and has not been identified or described in the study protocol and/or listed in the SmPC and Investigator’s Brochure.

*Note however that a documented AR may be described as ‘unexpected’ if it has occurred with greater frequency or severity that might otherwise have been expected.*
3.9 Reporting Responsibilities

3.9.1 NHS Trust Incident Reporting Procedures
The PI is responsible for ensuring that all adverse incidents, which involve NHS patients, staff, or facilities are reported in accordance with the relevant NHS Trust Incident Reporting Procedure.

3.9.2 Urgent Safety Measures
Urgent Safety Measures that are implemented immediately should be notified to all the Sponsor(s), REC, and, where appropriate, MHRA within 3 days of the measures being taken, along with the reasons for the measures being taken.

3.9.3 Adverse Events
AEs identified in the protocol as critical to the evaluation of the safety of the study should be reported in accordance with reporting requirements defined and documented in the protocol.

3.9.4 Serious Adverse Events
All SAEs/SARs and SUSARs should be reported to the Pharmacovigilance Sponsor (or delegated individual) within 24 hours of being made aware of the event. The immediate report may be made orally or in writing and shall be promptly followed by a detailed written report.

SAEs, SARs and SUSARs should be reported using trial specific report forms if available. The format of the report should use all the basic elements described in the European Commission: Detailed Guidance on the Collection, Verification and Presentation of Adverse Reaction Reports arising from Clinical Trials on Medicinal Products for Human Use. An example is given as Appendix 2.

SAE, SAR and SUSAR reports should be as complete as possible and should be signed and dated by the local Investigator. However, complete information may not be available within the given timeframes for reporting. In this case the initial report will contain as much information as is available at the time. The PI will be required to submit a follow-up report as soon as complete information becomes available. The PI is required to actively follow up all SAEs.

SAE, SAR and SUSAR reports must provide an assessment of causality at the time of initial reporting to the Pharmacovigilance Sponsor.

Note that it may be necessary to unblind the medication of the trial participant in order to make a definitive assessment of a SAR and to confirm a SUSAR. The protocol should set out the procedure for unblinding in such circumstances. The procedure for reporting SAEs, SARs and SUSARs where UoM is acting as the Pharmacovigilance Sponsor is set out in UoM Guidelines on Pharmacovigilance.

All SAE, SAR and SUSAR reports to the Pharmacovigilance Sponsor should be retained by the local Investigator in the Investigator Site File and/or Trial Master File.
Likewise all SAE, SAR and SUSAR reports received by the Pharmacovigilance Sponsor, together with any follow-up information, should be kept in the Sponsor File.

3.9.5 Out of hours
Out of hours procedures and contact information must be detailed in the protocol for all safety reporting. This may vary across sites where local processes differ. Out of hours provisions must also include unblinding activities, including any back up procedures for electronic systems where relevant.

3.10 Expedited Reporting of SUSARS to the main Research Ethics Committee (REC) and the MHRA

3.10.1 The Pharmacovigilance Sponsor is responsible for reporting SUSARs to the MHRA and the main REC (the REC that approved the trial), other relevant competent authorities and any other relevant organisations. Reporting responsibilities will normally be delegated to the CI or a Clinical Trials Unit. SUSARs must be reported to the MHRA electronically using the eSUSAR website via [https://esusar.mhra.gov.uk](https://esusar.mhra.gov.uk). Users of the system should be documented on the study delegation log. Registration to the eSUSAR website will be controlled through the Research Governance, Ethics and Integrity Office, the NHS co-sponsor or CTU.

3.10.2 For multicentre trials that began before the 1st May 2004, approval will have been granted from numerous RECs. In these situations the Pharmacovigilance Sponsor must nominate one of the RECs for all pharmacovigilance reporting.

3.10.3 All SUSAR reports faxed or emailed to the Pharmacovigilance Sponsor and any follow-up information should be kept by the local Investigator in the Investigator Site File (ISF) and/or trial master file.

3.10.4 All SUSAR reports received by the Pharmacovigilance Sponsor, together with any follow-up information, should be kept in the Sponsor file.

3.11 Expedited Reporting of other events

3.11.1 The following safety issues will also be reported to the Pharmacovigilance Sponsor(s) by the Investigator in an expedited fashion:

- An increase in the rate of occurrence or a qualitative change of expected SAR, which is judged to be clinically important.
- Post-study SUSARs that occur after the trial subject has completed a clinical trial.
- New events related to the trial or the development of the investigational medicinal products and likely to affect the safety of the subjects.
- Recommendations of the Data Monitoring Committee where relevant for the safety of trial subjects.
3.11.2 If identified, the local Investigator must report these safety issues to the Pharmacovigilance Sponsor in the same way as described in section 3.9

3.12 Other Reporting Requirements

3.12.1 In multicentre trials the Pharmacovigilance Sponsor is responsible for informing Investigators at all participating sites of any reported SUSARs.

3.12.2 Reports sent to the Investigator regarding SUSARs from other trials of the same medicinal product must be reviewed by the Investigator and acted upon if appropriate. All copies of such SUSAR reports must be kept in the ISF and copies sent to the Chief Investigator for the TMF.

3.12.3 The Chief Investigator is responsible for submitting annual safety reports to all Sponsors, the MHRA and the main REC on the anniversary of the Clinical Trial Authorisation approval.

3.12.4 The CIs of other relevant trials must be informed if any AEs from a trial may have potential impact on their open trials.

3.12.5 All major deviations and/or breaches must be recorded and reported as per SOP12 Reporting of Serious Breaches.

3.12.6 Minor incidents and issues across all elements of the trial should be reported to the Sponsor via the monthly and quarterly Sponsor reporting channels. Where deemed serious/necessary the Sponsor should be approached outside of this reporting timeframes. These will be reviewed and actioned by the Research, Governance, Ethics and Integrity team. Where resolution cannot be made CTMG will be consulted.

3.13 Pregnancy Reporting

3.13.1 Pregnancy is not considered an AE or SAE. However the local Investigator must collect pregnancy information for female trial subjects or female partners of male trial subjects who become pregnant while participating in a study.

3.13.2 The Investigator should record the information on a Pregnancy Notification Form and send this to the Pharmacovigilance Sponsor within 14 days of being made aware of the pregnancy.

3.13.3 Any pregnancy that occurs in a trial subject or a trial subject’s partner during a trial should be followed to outcome. In some circumstances, it may be necessary to monitor the development of the newborn for an appropriate period post-delivery.
3.14 Role of the non-pharmacovigilance Sponsor

The UoM has the following role in trials in which it is the non-pharmacovigilance Sponsor:

- Establish prior to commencement of the trial that appropriate arrangements are in place by the pharmacovigilance Sponsor to receive and deal with all relevant reports (outlined above).
- To receive a copy of the annual safety report.
- To check with the pharmacovigilance Sponsor that the required onward reporting has taken place.
- To keep a copy of all pharmacovigilance documentation in the Sponsor file.

4.0 Appendices

Appendix I  Summary of Investigators/Sponsors Responsibilities
Appendix II  Example serious adverse event and adverse reaction report form
Appendix III  Drug Safety Update Report
Appendix IV  Sponsor notification of SUSAR to Investigators

5.0 References:

- University of Dundee SOP for identifying, recording and reporting adverse events for clinical trials of Investigational Medicinal Products.
- World Medical Association for Declaration Helsinki Ethical Principles for Medical Research Involving Human Subjects
- Medicines for Human Use (Clinical Trials) Regulations 2004
- Cardiff University SOP for the managing and reporting of research related Adverse Events in Clinical Trials of Investigational Medicinal Products
Appendix I:

Responsibilities of the Investigator – any Investigator at any site

<table>
<thead>
<tr>
<th>In respect of:</th>
<th>Is responsible for:</th>
<th>Recording/reporting to:</th>
<th>By (timescale)</th>
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<tbody>
<tr>
<td>Recording notification of AEs</td>
<td>Asking subjects about AEs at each study visit or via an emergency ‘hot line’</td>
<td>Recording in CRF, as required by protocol</td>
<td>When updating CRF</td>
</tr>
<tr>
<td>AE not identified in protocol as not requiring to be reported</td>
<td>Deciding if it is ‘serious’ i.e. an SAE</td>
<td>Sponsor if defined as SAE</td>
<td>Immediate, but see * below</td>
</tr>
<tr>
<td>SAE</td>
<td>Follow-up report</td>
<td>Sponsor with detailed written report</td>
<td>At a convenient time**</td>
</tr>
<tr>
<td>AE identified in protocol as critical to safety evaluation</td>
<td></td>
<td>Sponsor</td>
<td>As set out in the protocol</td>
</tr>
<tr>
<td>SAE that resulted in death</td>
<td>Providing further information</td>
<td>Sponsor, on request</td>
<td>Promptly as requested</td>
</tr>
<tr>
<td>All SAEs</td>
<td>Making decisions about causality</td>
<td>Sponsor, to indicate SAR</td>
<td>Include in detailed written report, above</td>
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Responsibilities of the Pharmacovigilance Sponsor

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<th>In respect of:</th>
<th>Is responsible for:</th>
<th>Recording/reporting to:</th>
<th>By (timescale)</th>
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</thead>
<tbody>
<tr>
<td>SARs</td>
<td>Deciding if expected or unexpected (may consult and agree with investigator)</td>
<td>If expected – record as SAR If unexpected – expedited report of SUSAR</td>
<td>See below</td>
</tr>
<tr>
<td>Reports of SUSARs, fatal or life-threatening</td>
<td>Expedited reporting</td>
<td>Co-sponsor MHRA and the Ethics Committee***</td>
<td>Within 7 days of being notified</td>
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<tr>
<td>Above fatal or life-threatening SUSARs</td>
<td>Providing any other relevant information that becomes available</td>
<td>Co-sponsor, MHRA and the Ethics Committee***</td>
<td>Within a further 8 days</td>
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<tr>
<td>Other SUSARs, non-fatal, non-life threatening</td>
<td>Expedited reporting</td>
<td>Co-sponsor, MHRA and the Ethics Committee***</td>
<td>Within 15 days of being notified</td>
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<tr>
<td>All SUSARs</td>
<td>Circulating information</td>
<td>All Investigators in on-going trials of the drug in which they act as Sponsor</td>
<td>As set out in the protocol</td>
</tr>
<tr>
<td>All SAEs, SARs and maintaining detailed records</td>
<td>Maintaining detailed records</td>
<td>MHRA and Ethics Committee***</td>
<td>Annually (or end of study if &lt; 1)</td>
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### SUSARs reported by Investigators

| All SAEs, SARs and SUSARs reported by Investigators | Making above detailed record available | MHRA on receipt of a written request | Anytime, as requested |

* When reporting SAEs to Sponsor, consider the urgency of the situation in deciding what is meant by ‘immediate’. It might mean at a convenient time on the following working day but, clearly, investigators will only become aware of some adverse events sometime after they occur (depending upon frequency of study visits).

** Note that the Sponsor has a legal obligation to expedite reports of SUSARs to MHRA i.e. with 7/15 days.

*** Even in multi-site studies, the Sponsor need notify ONLY the ethics committee that provided a favourable opinion concerning the study. Do NOT circulate to ALL other committees whose role was restricted to Site Specific Assessment only.
Appendix II:

**EXAMPLE:** SERIOUS ADVERSE EVENT and ADVERSE REACTION REPORT

DETAILED FOLLOW-UP REPORT BY INVESTIGATOR TO SPONSOR

**PART 1: ABOUT THE SERIOUS ADVERSE EVENT (SAE)**

**Ethics Committee reference:** ………………………

**EuDraCT No:** ………………………

<table>
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<th>Start date (Date on CTA approval notice):</th>
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<tr>
<th>Chief Investigator:</th>
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**Sponsor:** ……………………………………………………………………………………

(Either UoM or joint UoM/NHS) (Only use this form if the UoM responsible for pharmacovigilance)

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<tr>
<th>Subject details:</th>
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| Initials …… Trial code ………………. Sex … Date of birth: ……….. Age …… |
|----------------|----------------|---------|---------------|
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<table>
<thead>
<tr>
<th>Description of Adverse Event (incl: signs, symptoms, relevant lab tests, onset, duration). Other relevant history (eg, diagnoses, allergies, pregnancy within last month, etc)</th>
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<tbody>
<tr>
<td>(Indicate if a new event or continuation of previously reported event)</td>
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<tr>
<th>Assessment of ‘seriousness’ (tick relevant category):</th>
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<tbody>
<tr>
<td>Death † † Life-threatening: † † Hospitalisation: †</td>
</tr>
<tr>
<td>Prolonged hospital stay: † Persisting disability/incapacity: †</td>
</tr>
<tr>
<td>Congenital anomaly/birth defect: † Otherwise considered serious: †</td>
</tr>
</tbody>
</table>

(Note: Investigator may consider the event to be otherwise serious if, for example, it required remedial active intervention or treatment).
Action/outcome: (eg, unblinding, subject withdrawn, event resolving, ongoing, etc)

Do you suspect a link between the above event and a study drug?

If YES, this is a SAR or SUSAR and you should complete PART 2, overleaf. Otherwise sign overleaf and return as requested.
PART 2: ABOUT THE SERIOUS ADVERSE REACTION (SAR or SUSAR)
(Complete ONLY if you suspect a link to a study drug. Otherwise leave blank and sign and return, as requested)

Approved name: ................................ Proprietary/trade name ......................

Indicate your level of suspicion that the event is related to the trial drug? (Tick box)

Possibly related  |  Probably related  |  Definitely related  |

Assessment of ‘expectedness’, i.e., whether or not described as an adverse drug reaction in the Summary of Product Characteristics or Investigator’s Brochure (but note that the Pharmacovigilance sponsor will independently assess expectedness)

Expected  |  Unexpected  |

(Note that known adverse reactions must be reported as being UNEXPECTED if thought to occur at greater frequency or with greater severity than expected.)

Date drug commenced: ..........  Date drug stopped: ..........  Doses taken .......

Daily dosing schedule .......................  Indication for use

..........................

List concomitant drug therapy (incl: over-the-counter medicines, herbal remedies, etc)

Information on manufacturer/supplier

Pharmaceutical manufacturer name/address

Hospital pharmacy (if supplied via this route)

Batch number or other manufacturer’s control number: .................................

Name of person completing this report (print): ..............................  Date: ..........  

Send the completed form to:

Research Office
Christie Building
University of Manchester
Oxford Road
Manchester M13 9PL

research-governance@manchester.ac.uk
APPENDIX III

DRUG SAFETY UPDATE REPORT (DSUR)

[REPLACES THE FORMER ANNUAL SAFETY REPORT TEMPLATE]

SEE UoM SOP DSUR for detailed information

The DSUR should take into account all new safety information received during each annual period.

Submission is now made using CESP (Common European Submission Portal).
APPENDIX IV

SPONSOR NOTIFICATION OF SUSAR TO ALL INVESTIGATORS

The University of Manchester

Research Governance and Integrity Team
Christie Building
University of Manchester
Oxford Road
Manchester M13 9PL

Tel: 0161 275 2725

Date

Dear Chief Investigator

NOTIFICATION OF SUSAR BY PHARMACOVIGILANCE SPONSOR

This letter has been sent to you as the Chief Investigator in a clinical trial* involving the investigational drug, ……………………. and for which University of Manchester is acting as the pharmacovigilance Sponsor.

* Title of clinical trial

Its purpose is to inform you of a SUSAR report received in another study for which University of Manchester is acting as pharmacovigilance Sponsor and in accordance with Part 5 of The Medicines for Human Use (Clinical Trials) Regulations 2004.

Insert a summary of the SUSAR to include:

• Suspect drug, dosage form and dose
• Indications for use in the clinical trial
• Nature of the SUSAR (include onset, duration, outcome)

Please inform any co-investigators of this notification. You are not required to take any further action.

Yours sincerely

Dr Mohammed Zubair