ECTU Central Office SOP ECTU_CL_10: Identification, Recording and Reporting of Adverse Events and Serious Adverse Events for Clinical Trials of Investigational Medicinal Products (CTIMPS) For Commercial Trials

Version No: 4.0
Effective Date: 21 July 2020

Authorship and Approval

<table>
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<tr>
<th>Name and Designation</th>
<th>Author/Reviewer/Approval</th>
<th>Date</th>
<th>Signature</th>
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<tr>
<td>Kate Covil, Research Nurse</td>
<td>Reviewer</td>
<td>07 July 2020</td>
<td>See retained approval email dated 07 July 2020</td>
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<tr>
<td>Debbie Hamilton, Research Nurse</td>
<td>Reviewer</td>
<td>07 July 2020</td>
<td>See retained approval email dated 07 July 2020</td>
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<tr>
<td>Debbie Alexander, Trial Team Manager (clinical)</td>
<td>Author/Approval</td>
<td>07 July 2020</td>
<td>See retained approval email dated 07 July 2020</td>
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Document Revision History

<table>
<thead>
<tr>
<th>Version No</th>
<th>Date</th>
<th>Summary of Revisions</th>
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<tbody>
<tr>
<td>1.0</td>
<td>30 June 2015</td>
<td>Initial creation/new document</td>
</tr>
<tr>
<td>2.0</td>
<td>28 August 2017</td>
<td>Updated at scheduled review. Section 2.1 Definitions now section 3. Subsequent sections renumbered accordingly. Reference to ACCORD SOP CR005 added to section 6</td>
</tr>
<tr>
<td>3.0</td>
<td>30 May 2018</td>
<td>Section 4.4 updated after recommendations at MHRA inspection. Minor alterations to section 1 and 2. Document moved to new template. Minor formatting changes throughout.</td>
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<tr>
<td>4.0</td>
<td>21 July 2020</td>
<td>Change of title to include ‘for commercial trials’ Minor word changes throughout,</td>
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1. PURPOSE

To allow ongoing safety evaluation of a CTIMP, all adverse events (AEs) and Serious Adverse Events (SAEs) experienced by patients following administration of a study drug, whilst participating in a clinical trial, will be reported to the sponsor in a manner appropriate to the nature of the event and in accordance with the study protocol or as documented in a Clinical Trial Agreement.

Adverse Event (AE) and other safety event identification, recording and reporting procedures will comply with the requirements of the Medicines for Human Use (Clinical Trial) Regulations 2004/1031 as amended and Good Clinical Practice (GCP).

This Standard Operating Procedure (SOP) describes the procedure for identifying, recording and reporting safety reporting of all patients taking part in a commercial CTIMP trial.

2. SCOPE

This SOP applies to all the Clinical staff, delegated to a study, who are responsible for identifying, recording and reporting AEs and SAE’s for commercially sponsored trials.

3. PROCEDURE

3.1 Definitions

An Adverse Event, Adverse Reaction, Serious Adverse Event and Serious Unexpected Adverse Reaction are defined as the following unless otherwise stated in the protocol:

3.1.1 Adverse Event (AE)

Any untoward medical occurrence in a clinical trial patient or subject administered an Investigational Medicinal Product (IMP) which does not necessarily have any causal relationship with this treatment.

3.1.2 Adverse Reaction (AR)

Any untoward and unintended response to an IMP which is related to any dose administered to a trial participant

3.1.3 Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)

Any untoward medical occurrence that at any dose

- Results in death of the clinical trial participant
- Is life-threatening*
- Requires inpatient hospitalisation^ or prolongation of existing inpatient hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect
- Results in any other significant medical event not meeting the criteria above

* Life-threatening in the definition of an SAE or SAR refers to an event where the participant was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it were more severe.

^ Any hospitalisation that was planned prior to randomisation will not meet SAE criteria, unless otherwise stated in the study protocol. All hospitalisations not planned following randomisation should be reported as an SAE unless otherwise stated in the protocol
3.1.4 Suspected Unexpected Serious Adverse Reaction (SUSAR)

Any adverse reaction that is classified as serious, is suspected to be caused by the IMP and is not consistent with the IMP information in the Summary of Product Characteristics (SmPC) or Investigator’s Brochure (IB).

3.2 Identification of Events

Adverse Events or Serious Adverse Events may be identified following medical review of laboratory or safety data, or through symptoms reported by the patient, following direct questioning by the Principal Investigator (PI) or research nurse. All AEs will be recorded from the time the patient signs informed consent, unless otherwise stated by the protocol.

3.3 Assessment and Reporting

All AEs/SAEs must be assessed for seriousness, causality, severity and expectedness by the Principal Investigator or another delegated suitably qualified physician who is in the research team and trained in the recording and reporting of AEs and SAEs. Refer to the study protocol for specific reporting criteria. For double blind studies all AEs/SAEs must be assessed as though the patient were taking IMP.

A full medical examination will be carried out if judged necessary by the Principal Investigator or suitably qualified study physician. If the event is judged to be an SAE/SAR/SUSAR it is subject to expedited reporting requirements. The protocol should define which SAEs should not be expedited to sponsor. It is the responsibility of the PI to report the SAE to the sponsor within 24hrs of becoming aware of the event.

Refer to study protocol for specific expediting and reporting procedures for SAEs/SAR/SUSARs.

The following minimum data elements should be included in the SAE/SUSAR reports:

- A valid EduraCT number (where applicable)
- A sponsor study number
- Subject study number
- Reporter e.g. PI or research nurse
- Details of IMP
- Causality assessment—must always be assessed by the PI or delegated study physician
- Full description of the event
- Medical history and concomitant medications
- Seriousness and expectedness*—Check individual protocol for specific reporting
- Dates of drug administration
- In case of death, date and cause of death
- Date PI/research nurse became aware of the event
- Whether the report is an initial or a follow up report

* The Reference Safety Information (RSI) should be used to assess expectedness and should be clearly identified in the protocol, this specifically references what AE’s are considered to be expected for that IMP.

3.4 Medical Treatment

The Principal Investigator can decide to treat the AE or SAE as required unless otherwise stated in the protocol, any medication prescribed should be recorded in the concomitant medication section of the CRF/eCRF and source document.
3.5 Recording Events

All AEs and SAEs must be documented in the subject’s pCRF/eCRF and source documentation by the study research nurse, Principle Investigator or delegated study physician. Any discussion with the Principal investigator/sub-Investigator with regards to seriousness, causality, severity and expectedness of AE’s or SAE’s must also be documented in the subjects’ source worksheets.

The subject’s GP and the ethics committee may be informed of any significant AEs/SAEs/SUSARs and details of any urgent safety measures included.

3.6 Follow-up

All AEs and SAEs should be followed up until resolution unless otherwise stated in the protocol.

3.7 Pregnancy

Pregnancy does not meet the definition of an SAE; however a congenital anomaly or birth defect is considered an SAE. When pregnancy occurs in a trial in either a female patient or in a female partner of a male patient this should be followed up until the end of the pregnancy and outcome. See specific protocol instructions for pregnancy notification procedures.

4. RELEVANT DOCUMENTS AND REFERENCES


Medicines for Human Use (Clinical Trial) Regulations 2004/1031 as amended.