

Standard Operating Procedure CCTU/SOP003

Development Safety Update Report and Annual Progress Reporting for Investigator Teams

1. Scope

The preparation and submission of the Development Safety Update Report and the Annual Progress Report is delegated by the Sponsor to the Chief Investigator of CTIMPs sponsored by CUH or jointly sponsored by CUH and the University of Cambridge (**Trust-Sponsored**).

2. Purpose

This SOP is designed to ensure that investigators are aware of their responsibilities regarding the provision and submission of Safety Reports as required by *regulation 35 The Medicines for Human Use (Clinical Trials) Regulations* and Annual Progress Reports as a condition for continuous ethical favourable opinion.

3. Definitions and Abbreviations

The headings below contain the definitions of terms and meaning of abbreviations used within the document.

Common abbreviations and definitions can be found in CCTU/INF001 Common Abbreviations and Definitions.

3.1. Definitions

Term	Definition
Trust-Sponsored	Sponsored by Cambridge University Hospitals NHS Foundation Trust (CUH) or sponsored by CUH jointly with The University of Cambridge
Development Safety Update Report (DSUR)	The Development Safety Update Report is the new format for the annual safety reporting (having come into affect 01 September 2011) and focuses specifically on new safety information identified during the reporting period with a view to ongoing risk-benefit analysis.
Adverse Event (AE)	Any untoward medical occurrence that happens to a patient or research participant to whom investigational medicinal Product has been administered in a clinical trial, which may or may not necessarily have causal relationship with the research being

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	undertaken.
Adverse Reaction (AR)	An untoward and unintended reaction that is considered to be related to the administration of the IMP.
Serious Adverse Event (SAE)	Any AE or effect that at any dose: <ul style="list-style-type: none">• Results in death• Is life threatening• Requires hospitalisation or prolongation of existing hospitalisation• Results in persistent or significant disability/incapacity• Is a congenital anomaly/birth defect• Is an otherwise significant event
Serious Adverse Reaction (SAR)	An SAE that is considered to be possibly, probably or definitely related to the IMP.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	An adverse reaction , which is both serious and unexpected, i.e. the nature or severity of which is not consistent with the applicable product information and which fulfils one or more of the criteria listed above for SAE.
Development International Birth Date	The anniversary of the clinical trials authorisation from the MHRA

3.2. Abbreviations

Abbreviation	Meaning
CUH	Cambridge University Hospitals NHS Foundation Trust
CTO	Clinical Trials Officer
CTA	Clinical Trials Authorisation
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SUSAR	Suspected Unexpected Serious Adverse Reaction
DSUR	Developmental Safety Update Report
ASR	Annual Safety Report
APR	Annual Progress Report
CTIMP	Clinical Trial of Investigational Medicinal Product
MHRA	Medicines and Healthcare Products Regulatory Agency
REC	Research Ethics Committee
IMP	Investigational Medicinal Product
NRES	National Research Ethics Service
DIBD	Development International Birth Date

4. Undertaken by

This SOP applies to Chief Investigators and their study teams involved in the management of Trust sponsored CTIMPs

5. Items Required

Development Safety Update Template/Form CCTU/TPL012

ICH Development Safety Update Report Guidance

CTIMPs Safety Report Form for sending DSUR to the REC:

<http://www.nres.npsa.nhs.uk/applications/after-ethical-review/safetyreports/safety-reports-for-ctimps/submitting-safety-reports-to-the-rec/>

Annual Progress Report Form for CTIMPs – from REC website

<http://www.nres.npsa.nhs.uk/applications/after-ethical-review/annual-progress-reports/>

6. Summary of Significant Changes

The Annual Safety Report has been replaced by the Development Safety Update Report as of the 01st Sept 2011

7. Method

The following sections provide a description of the processes to be followed when implementing this document's procedures.

7.1. Regulations

Refer to "ICH guideline E2F: Note for guidance on development safety update reports" available online and from the CCTU.

The Development Safety Update Report (DSUR) for CTIMPs should be submitted **within 60 days** of the Development International Birth Date (DIBD), which for the purposes of the trials Sponsored solely or jointly by CUH will be the **anniversary of the clinical trials authorisation from the MHRA**. A copy of the DSUR must also be sent to the REC accompanied by the REC CTIMP Safety Report Form (see 7.5).

7.2. The Development Safety Update Report (DSUR)

- Chief Investigators will receive a reminder email from the CCTU on the anniversary of the trial's Clinical Trials Authorisation

- The assigned CTO in the CCTU will send -a copy of the DSUR template, containing guidance for completion to the CI and trial team, along with confirmation of the submission timelines
- The DSUR contains sections which need to be completed by the CI/trial team and sections for the Sponsor to complete
- The CTO should be the point of contact going forward for all questions/queries related to the completion and submission of the DSUR
- The CI or trial team designee should complete those sections marked for their attention in the template
- The CTO will then complete those sections that are for the Sponsor's attention and check that the instructions in the Template have been appropriately followed
- The draft DSUR must be provided to the CTO 3 weeks prior to the submission deadline. Any delay in providing this, without prior agreement of the CCTU will be escalated as a non-compliance to the Sponsor
- Any necessary alterations agreed are made by the CI or CTO in the relevant sections as appropriate
- The final DSUR will then be reviewed and signed by the Sponsor's Representative in the CCTU
- The CTO will burn the DSUR and accompanying documents (Any abstracts of papers that were discussed in the DSUR, the cover letter, new Safety Reference information in the form e.g.: Investigator Brochures or Summaries of Product Characteristics etc) onto a CD and will send this to the MHRA.
- The CTO will provide the CI/trial team with a copy of the full DSUR submission for the TMF and submission to the REC
- It is the CI's responsibility to provide the DSUR and accompanying documents (including the NRES Safety Report Form) to the REC which gave favourable opinion for the trial, electronically either on CD or via email

7.3. Short Term Trials

- For short term trials (lasting less than 1 year from CTA approval) there is no need to submit a DSUR, all safety information should be included in the trial report submitted within 1 year of end of trial declaration.

7.4. The Annual Progress Report

It is a requirement for continued favourable opinion from the REC that an Annual Progress Report (APR) be submitted annually, within 30 days of the **anniversary date when favourable opinion for the study was received from the REC.**

The APR is submitted to the REC ONLY. The Trust has delegated the responsibility of the APR completion to the Chief Investigators.

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The Annual Progress Report Form for CTIMPs published on the NRES website **must** be used:

<http://www.nres.nhs.uk/applications/after-ethical-review/annual-progress-reports/>

- Chief Investigators will receive a reminder email from the CCTU on the anniversary of the Favourable Opinion from the REC for the trial
- If any extension to the duration of the trial is required, this must be included in the APR as notification of the extension to the REC
- A final, signed copy of the APR and covering letter must be submitted to the CTO for review and inclusion in the Sponsor file

7.5. Waiver of Requirement to Submit an APR

- When a trial has closed to recruitment and all patients have completed their intervention phase but will continue to be followed up for a long period of time with minimal involvement, a waiver of the requirement to send an APR can be requested
- This must be requested in writing to the chairman of the REC
- The response should be sought in writing and filed in the Trial Master File and provided to the Sponsor

7.6. Submission of Reports

Ensure that all the original reports are signed and dated by the CI

DSUR Submission	Annual Progress Report Submission
<u>Send DSUR to the MHRA on disc</u> Refer to the website for current requirements	<u>Send completed and signed APR form to the REC in hard copy</u>
Include covering Letter	Include covering Letter
Send a copy of the DSUR to the REC on disc or via email accompanied by the REC CTIMP safety report form.	
Make two copies of all the signed original documents, one set for filing in the TMF and send the second set to the CCTU	

- For multi-centre trials the CI is responsible for the distribution of the DSUR and APR to all participating sites refer to R&D/SOP001 CTIMP Delegation of Roles and Responsibilities.

8. Monitoring Compliance with and the Effectiveness of this Document

a. Process for Monitoring compliance and Effectiveness

As part of routine monitoring visits, audit and inspection

b. Standards/Key Performance Indicators

This process forms part of a quality management system. Documents are reviewed every two years

9. References

The Institute of Clinical Research, 2008, Abbreviations used in Clinical Trials.

The UK Clinical Trial Regulations

www.legislation.gov.uk/ukxi/2004/1031/contents/made

10. Associated Documents

See section 5

11. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

12. Disclaimer

It is the user's responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

Review date	2 years (or earlier in light of new evidence) from approval date
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Supersedes:	A S R and Annual Progress reporting CCTU/SOP003 v1
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