

## STU-SOP-TM-007 – Standard Operating Procedure on Development Safety Update Reports for CTIMPs

<b>Version No:</b>	5	<b>Effective Date:</b>	10-Apr-2026
<b>Description of changes:</b>	SOP reviewed in light of clinical trial regulations 2025 and GCP updates. Specific references to QPulse as the QMS have been removed. We now only refer to a QMS system. Update to APR reporting requirements which are no longer needed as per HRA website		

List of Abbreviations	
<b>APR</b>	Annual Progress Reports
<b>ASR</b>	Annual Safety Report (aka the DSUR)
<b>CESP</b>	Common European Submission Portal
<b>CI</b>	Chief Investigator
<b>CTA</b>	Clinical Trial Authorisation
<b>CTIMP</b>	Clinical Trial of an Investigational Medicinal Product
<b>DIBD</b>	Development International Birth Date
<b>DMC</b>	Data Monitoring and Ethics Committee
<b>DSUR</b>	Development Safety Update Report
<b>EMA</b>	European Medicines Agency
<b>HCRW</b>	Health and Care Research Wales
<b>HRA</b>	Health Research Authority
<b>IB</b>	Investigator Brochure
<b>IMP</b>	Investigational Medicinal Product
<b>MHRA</b>	Medicines and Healthcare products Regulatory Agency
<b>MP</b>	Medicinal Product
<b>REC</b>	Research Ethics Committee
<b>RSI</b>	Reference Safety Information
<b>SmPC</b>	Summary of Product Characteristics
<b>SOP</b>	Standard Operating Procedure
<b>STU</b>	Swansea Trials Unit
<b>SU</b>	Swansea University
<b>TM</b>	Trial Manager
<b>TMF</b>	Trial Master File

### 1. Purpose and Definitions

This Standard Operating Procedure (SOP) describes the procedure of drafting and submission of full or short form Development Safety Update Reports (DSURs) for Clinical Trials of Investigational Medicinal Products (CTIMPs) to the Medicines and Healthcare products Regulatory Agency (MHRA), or other regulatory bodies.

Definitions	
<b>Interventional Clinical Research Projects</b>	Involve humans as participants and an invasive experimental element that may or may not allocate the treatment by randomisation. Such projects involve a single person or groups of people, using material or behaviours (previously collected or not) from those people. They include surgical and

	imaging trials, trials providing food supplements or herbal remedies, cosmetics, microorganisms or medicines (whether licensed or not), device trials (whether CE marked or not), used in usual or non-usual clinical practice.
<b>Non-interventional Clinical Research</b>	Involve humans as participants but does not involve an invasive experimental element and may or may not allocate the treatment by randomisation. Such projects involve a single person or groups of people, using material or behaviours (previously collected or not) from those people. They include questionnaire or qualitative studies, observation or cohort studies and retrospective data analysis.

## 2. Background

Since October 2024 the HRA website states that there is no requirement for Annual Progress Reports (APRs) to be submitted to NHS RECs. However, CTIMPs do require an annual safety report referred to as a Development Safety Update Report (DSUR).

For certain Type A projects authorised under the Clinical Trial Notification Scheme a shortened DSUR may be used in lieu of the detailed full DSUR required for Type B and C projects.

Annual DSURs should be submitted whether or not recruitment has commenced. For a trial with a duration of less than 12 months and that concludes before the end of the reporting year, no DSUR is required.

## 3. Roles and Responsibilities

**The Sponsor** is responsible for ensuring that the APR and appropriate DSUR (when required) are completed for all research projects.

**The Chief Investigator (CI)** is responsible for overseeing the completion of the APR and DSUR and confirming the accuracy of content while ensuring that the blind is maintained for ongoing projects. The CI also has responsibility for checking that the Reference Safety Information (RSI), for MP research projects, remains applicable.

**The Trial Manager (TM)** or delegate is responsible for coordinating the completion of the APR and DSUR, liaising with the Sponsor and ensuring that only unblinded personnel review the final DSUR while blinded personnel review only initial drafts. The TM will also be responsible for coordinating the review of the RSI documents.

**External use of SOP:** This SOP and Associated Documents (ADs) may be used for research projects not adopted by STU where Swansea University (SU) staff and associated NHS organisations require guidance. In such instances, oversight responsibility for any associated tasks will not be the responsibility of STU.

## 4. Procedure

### 4.1 Annual Progress Reports

Historically, the first APR was due 12 months after the date of the favourable opinion for any research project and had to be submitted within 30 days of this date.

On 1 August 2024 the requirement to submit APRs for studies that had received a final opinion from any UK REC was removed. This change was first introduced in England and Wales on 1 June 2024 and then in Scotland and Northern Ireland on 1 August 2024.

For research requiring only HRA and HCRW Approval you do not need to provide a progress report.

#### 4.2 Development Safety Update Report (CTIMPS only)

Following a Clinical Trial Authorisation (CTA) involving a Medicinal Product (MP), a sponsor/ CI as delegate must submit an annual DSUR (also known as the Annual Safety Report):

- Type A CTIMPs – authorised under the Clinical Trial Notification Scheme and not part of a multi-study MP development programme may submit a shortened DSUR in the form of the APR. A cover letter to the MHRA and REC should state that the APR is in lieu of a full DSUR and include the EudraCT and Clinical Trial Authorisation (CTA) reference numbers and a list of all Serious Adverse Reactions.
- Type B or C CTIMPs – must submit a full DSUR containing all required information as detailed in the DSUR template (STU-AD-FRM-023) to the MHRA (or equivalent regulator).

A DSUR is required every 12 months after the date of a CTA for NHS and academic Sponsors. Alternatively, it may be aligned to the Developmental International Birthdate (DIBD) of the MP when the manufacturer is submitting the DSUR. The report must list all suspected serious adverse reactions in the reporting period, both expected and unexpected and summarise any issues affecting safety of participants.

The European Medicines Agency (EMA) provide detailed guidance of the requirements for reporting to all regulatory authorities and ethics committees in each member state. This guidance document can be found as STU-AD-GDN-008.

Where possible, the responsibility for the completion of the DSUR should be with the manufacturer/supplier of the MP but the CI and TM will typically complete the template DSUR and Sponsor will review it prior to submission.

Where the research team do not have access to information required for the DSUR (e.g. manufacturing issues, marketing status, non-clinical data) this should be recorded as 'not applicable for this report'. DSUR sections in the template should not be removed or left blank.

For blinded ongoing projects, blinded personnel will only review an initial draft of the DSUR. The final version of the DSUR with unblinded safety data will be reviewed only by unblinded personnel e.g. by the Data Monitoring Committee (DMC). This process shall be coordinated by either the TM or delegate to ensure that the blind is maintained. Sponsor will allocate unblinded personnel to review when appropriate.

The shortened DSUR can only be submitted for individual CTIMPs. A Sponsor can still submit a single full DSUR for multiple research projects involving one MP.

A full DSUR should be used as the annual submission to regulatory bodies outside of the UK. The short form DSUR would not be acceptable.

##### 4.2.1 Development Safety Update Reports for trials pre-dating the combined review approvals process.

For CTIMPs not submitted for initial approval via the combined review (CWOW) process the DSUR should be submitted to the MHRA as per the guidance on the MHRA website and to each REC responsible for a trial of the IMP (use separate covering form for each).

DSURs or any other safety reports e.g. expedited adverse reactions, that are submitted to the REC should be accompanied by a completed REC CTIMP Safety Report form. The most recent version of the form will be available on the HRA website

<http://www.hra.nhs.uk/resources/during-and-after-your-study/nhs-research-ethics-committee-rec-ctimp-safety-report-form/>.

#### **4.2.2 Development Safety Update Reports for trials approved using the combined review approvals process.**

CTIMPs submitted via combined review can submit DSURs to the MHRA via CWOW. There is no requirement to separately notify the REC, the MHRA will liaise with the REC if deemed appropriate.

#### **4.3 Multiple Projects involving one medicinal product**

Where there is involvement with several CIs, the Sponsor will be responsible for recognising and ensuring collaboration in the completion of one or several DSURs for the MP as the regulations allow.

Where STU are involved in the multiple research projects there will be coordination with relevant TMs over responsibility for completion of the DSUR. Where STU are not involved in all research projects there will be liaison with the Sponsor over STU involvement in the multiple project DSUR or the drafting of separate DSURs.

If a DSUR submission incorporates more than one research project by the same Sponsor, the earliest CTA authorisation date may be used as the basis for the annual completion date

When unblinding of data are required, each DMC will review their own project data. The TM or delegate will compile the data into the final report. Each DMC will be asked to comment on the near final / final document before submission. The blind should be maintained for all projects.

#### **4.4 Review and Approval of Development Safety Update Reports by Sponsor**

The Sponsor requirements for review of DSURs should be followed. Often the requirements are the CI or delegate shall forward the draft DSUR (CTIMPS only) to the Sponsor or delegate at least 2 weeks prior to the submission date. The Sponsor shall review and confirm whether the submission is acceptable or request changes and further review.

When involved, the Sponsor will advise the CI (or delegate) in writing when the review has been completed.

#### **4.5 Submission Timelines, Process and Documentation**

The Sponsor timelines for review and submission of DSURs should be followed. It is usually the responsibility of the CI to submit all reports for review.

DSURs and shortened DSURs must be submitted to the MHRA portal for which you need to register via *Register to make submissions to the MHRA* - GOV.UK ([www.gov.uk](http://www.gov.uk)) using the Human Medicines Tile.

Prior to submission, the financial details for payment of the amendment fee must be included in the covering letter. Fees can be found at <https://www.gov.uk/government/publications/mhra-fees/current-mhra-fees#clinical-trials-application-fees> and methods for payment can be found at <https://www.gov.uk/guidance/make-a-payment-to-mhra>.

Submissions to other EU regulatory bodies are via the Common European Submission Portal (CESP) via <https://cespportal.hma.eu>. Training slides are available on the use of the portal for registered users. When submitting a DSUR, please select “regulatory activity G0042 – Development Safety Update Reports”.

Submission details serve as evidence of DSUR submission in lieu of an acknowledgment.

DSURs must be submitted regardless of whether recruitment has begun, including an explanation when required of why there has been no recruitment.

For CTIMPs not approved using the combined review process, the REC documentation submitted directly to them will be authorised by the REC and they will return the completed form. This notification must be filed in the TMF.

#### **4.6 Reference Safety Information (RSI) Review**

The appropriate Investigator Brochure (IB) or Summary of Product Characteristics (SmPC) in effect at the start of the reporting period must be used as the RSI for the DSUR. The IB or SmPC used in MP projects require at least an annual review which is recorded on the DSUR template (STU-AD-FRM-023).

If the IB or SmPC have been revised during the reporting period and not previously submitted to the MHRA or other regulatory authority, a copy of the revised RSI must be provided as an attachment to the DSUR. If there is a substantial change to the RSI there will be a need to submit a substantial amendment (to both the REC and MHRA) to update the RSI in the protocol prior to implementing a change to the RSI.

It is recommended that the IB/SmPC review is undertaken immediately prior to the start of drafting the DSUR submission.

#### **4.7 Distribution and Filing**

For CTIMPS a signed copy of each DSUR must be filed in the TMF. For STU adopted research studies, if the TMF is accessible to personnel involved in the conduct of a blinded project and contains unblinded participant data, the signed copies will be retained by an unblinded representative until the end of the project when they will be inserted into the TMF.

Where a DSUR covers multiple projects, a copy must be held in each TMF. Evidence of the DSUR submission must be filed in the TMF.

## **5. References**

- Health Research Authority website (HRA) - <http://www.hra.nhs.uk/>
- Medicine and Healthcare products Regulatory Agency website (MHRA) - <https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/services-information>
- UK policy framework for health and social care research (2017) - <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/>
- UK Medicine for Human Use (Clinical Trials) Regulations 2025 - <https://www.legislation.gov.uk/ukxi/2025/538/contents>
- Common European Submission Portal (CESP) - <https://cesportal.hma.eu/Account/Login?ReturnUrl=%2f>

It is assumed that by referencing the principal regulations that all subsequent amendments are included in this citation.

## **6. Associated Documents**

Number	Title	Location
STU-AD-GDN-008	ICH guideline E2F on development safety update report	QMS
STU-AD-FRM-023	DSUR template	QMS