UNIVERSITY OF LEICESTER

Research Governance Office Sponsorship Standard Operating Procedures

Development Safety Update Report (DSUR) for Clinical Trials of Investigational Medicinal Products

SOP Reference	S-1014
Version and Date	V6.0 April 2026
Author	
Name	**Claire Fitzpatrick**
Job Title	**Research Quality Assurance Officer**
Name	**Kyla Harrington**
Job Title	**Clinical Trials Governance Manager**
Reviewer/Approver	
Name	**Dr Cat Taylor**
Job Title	**Head of Research Governance**
Signature	
Date	**28 April 2026**
Effective Date*	28 April 2026
Next Review Date	April 2029

1.0 Introduction and Scope

For each Investigational Medicinal Product (IMP) tested in a clinical trial in the UK, the Sponsor must provide the licensing authority with an annual report on the safety of the participants receiving the product. This annual report should be in the form of a Development Safety Update Report (DSUR). This requirement includes IMPs tested in clinical trials approved via automatic authorisation (notifiable trials) or where the DSUR includes a combination of both notified and non-notified trials.

This Standard Operating Procedure (SOP) describes the procedures for the preparation, reporting and submission of a DSUR for Clinical Trials of Investigational Medicinal Products (CTIMPs; referred to as 'trial' hereafter) sponsored by University of Leicester (UoL). Where safety reporting/processing (i.e., DSUR writing and submission) is delegated to a 3rd party (i.e., CTU, Service Provider) this must be detailed in the protocol and risk assessment. Where applicable, a contract must be in place, and the procedures of the 3rd party will be followed.

2.0 DSURs

The main objective of a DSUR is to present a comprehensive annual review and evaluation of pertinent safety information collected during the reporting period related to a drug under investigation, whether or not it is marketed.

A DSUR should be concise and provide information to assure regulators that Sponsors are adequately monitoring and evaluating the evolving safety profile of the investigational drug. While the DSUR should not be used to communicate new safety issues (which should be done via updates of the investigator's brochure and, if applicable, via urgent safety measures (USM)) it should describe the actions taken to address safety concerns identified during the reporting period.

Actions to address safety concerns may include adding an event as an adverse event of special interest (AESI), additional safety assessments or additional timepoints for assessments already in place, more frequent Data Safety Monitoring Board/Committee (DSMB/C) oversight, an USM or temporary halt, as well as how the safety concern is communicated to locations and investigators.

DSURs are prepared per IMP rather than per trial, therefore, a single DSUR may cover multiple trials where a single IMP has been used across those trials. A trial specific DSUR may be accepted by exception, but advanced advice and approval must be sought from the MHRA.

For trials involving combination and multi-drug therapies section 2.5 of the Guidance on Development Safety Update Report (E2F) provides guidance. The sponsor should select the most appropriate option based on judgement, taking into account patient population, indication, formulation, etc., as well as the circumstances in which the clinical trials are being conducted and national or regional laws or regulations. The rationale for this decision should be provided in the report.

Submission of a DSUR is not required where an IMP is used in a single trial that has a duration of less than one year that concludes before the end of the reporting year (as defined below).

3.0 Procedure

3.1 Timelines and Important Definitions

The CI (or delegate) is responsible for ensuring that a DSUR is submitted annually for the duration of the trial, until the regulator has been notified of the end of the trial. The DSUR must be submitted to the licensing authority (but not the ethics committee) within 60 calendar days from the day after the end of the reporting year/data lock point (DLP).

For UoL Sponsored CTIMPs, a single annual DLP will be used in lieu of the international birth date and development international birth date as the anchor for DSUR submission timeframes. The DLP is defined as the anniversary of the Clinical Trials Application (CTA) authorisation date (i.e., the anniversary of MHRA/CA approval). Thus, the first DSUR will be produced on the first anniversary of MHRA/CA approval, taking into account the data generated in the preceding year.

Subsequent DSURs will then be produced annually thereafter on the anniversary of MHRA/CA approval taking into account the data generated in the preceding year. The reporting year is therefore the period between two anniversaries.

4.0 DSUR Preparation

4.1 Cover Letter

Each submission should include a cover letter with the following:

- a list of all the IRAS IDs (for trials approved through the combined review process) or EudraCT numbers (for trials not approved through the combined review process) of trials covered by the DSUR;
- an email address for correspondence; and
- the payment reference number in the format: DSUR-[22116 (this is the 5-digit MHRA company number)]-[IMP name]-[Payment date DD/MM/YYYY] (for a trial-specific DSUR using multiple IMPs, only include one IMP in the payment reference).

The MHRA only accept online payment of this fee before submission of an DSUR. Payment must be made via the dedicated DSUR page in the pay portal GOV.UK Pay. A receipt generated by the portal following payment will be sent by email to the payee. You must include this in the submission, in its original format as a standalone document that serves as proof of payment, along with the cover letter and DSUR.

Failure to provide evidence of payment will result in the submission being made invalid.

4.2 DSUR Template

The DSUR template (Appendix 1) follows the headings in section 3 of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guidance on Development Safety Update Report (E2F), and must be used. If a section is not applicable, this should be clearly indicated and the numbering/section retained (i.e., do not delete or change the numbering or section headings).

The MHRA website can be accessed for further details on the purpose, content and submission of DSURs.

Where DSURs need to be submitted to a CA outside the UK, the CI or their delegate is responsible for understanding and following the different submission requirements.

4.3 Expectedness Assessments and Reference Safety Information (RSI)

The Investigator Brochure (IB) or Summary of Product Characteristics (SmPC) contains the approved Reference Safety Information (RSI). It is important that the correct RSI is used to determine whether information received during the reporting period remains consistent with previous knowledge of the safety profile of the IMP. For expectedness assessments within the DSUR, **you must use the RSI that was valid at the start of the reporting period.**

Note: This may differ from the RSI used to assess the expectedness of an individual safety event.

If the approved RSI changes during the reporting period, you may need to reassess whether an event is expected for the DSUR. However **you do not need** to update individual SAE reports, the expectedness update relates to the DSUR only.

- A copy of the IB/SmPC in place at the beginning of the reporting period should be appended to the DSUR as evidence of the RSI that has been used for the report; the version and date should be listed within the DSUR.
- If the IB/SmPC has been revised during the reporting period, the updated version(s) should be appended to the DSUR and any significant safety-related changes should be listed in the relevant section of the DSUR; the version(s) and date(s) should be listed within the DSUR.

A review of the current IB/SmPC and RSI should be conducted at the same time as the DSUR submission, to aid with decision making about updating the approved RSI, please review Appendix 2 to SOP S-1023.

Where possible and where there is no safety risk to participants, updating the approved RSI should be aligned with the start of a new reporting period to avoid having multiple versions of the documents in place across a single reporting period and/or being used for single case reports.

Please liaise with the RGO if you think a change to the RSI is required.

4.4 Considerations for Blinded Trials

In the case of blinded trials and if individual SUSARs have been unblinded for the purposes of expedited reporting, these cases should be included in the DSUR in the unblinded format. Therefore, the line listings in the DSUR may contain both blinded and unblinded data. **Please note that you are not required to unblind data specifically for the purpose of the DSUR**. A robust process must be in place to protect the integrity of the blind.

For example, blinded personnel may only review an initial draft of the DSUR, prior to the addition of any unblinded information. The final review of the DSUR, with unblinded information included, must only be made by unblinded personnel.

Extra care should also be given to the storage of the final DSUR within the TMF; an alternative location may be more appropriate.

In all cases, the trial-specific unblinding process described in the protocol must be followed. This process identifies who is responsible for unblinding a participant in the event of a potential SUSAR and thus who holds the unblinded data for inclusion in the DSUR. It is the responsibility of all individuals involved in the DSUR to ensure the integrity of the blind is maintained as appropriate.

5.0 DSUR Completion and Submission

1. The Research Governance Office (RGO) will notify the Chief Investigator (CI) and Trial Manager/their delegate (as applicable) by email that the DSUR is due. Timelines for (1) the DLP, (2) submission to the RGO for Sponsor review, and (3) submission to the regulators will be clearly stated.
2. Draft reports **containing blinded information only** must be sent by the CI (or their delegate) to the RGO for Sponsor review.
3. Where unblinding for a SUSAR has occurred, the responsible unblinded personnel (as per the protocol) must add the unblinded information in to the report before it is sent to the RGO for Sponsor Review.
4. Where applicable, the RGO will add unblinded information.
5. Confirmation of RGO review and approval of the DSUR for submission to the regulators will be sent by email to the appropriate parties (determined by whether or not the DSUR contains unblinded data).
    a. Where the DSUR contains **blinded information only**, the CI (or their delegate) must then submit the DSUR.
    b. Where the DSUR contains **unblinded information**, the RGO (or another unblinded delegate) must then submit the DSUR.
6. Evidence of submission should be retained in the TMF and a copy sent to rgosponsor@le.ac.uk (where applicable).

To submit a DSUR to the licensing authority:

- if at least one of the clinical trials covered by the DSUR was approved through the combined review process, submit the report through IRAS. Guidance on

using IRAS to submit a DSUR can be found in the Step-by-step guide to using IRAS for combined review.

- if all of the clinical trials covered by the DSUR were approved through separate applications to the licensing authority and the ethics committee, submit the report through MHRA Submissions.

Contact the MHRA if there are issues with entering an IRAS ID for non-combined review trials on the IRAS platform.

7. The CI (or delegate) must ensure that, as appropriate, a copy of all completed documentation*, and where applicable/available, evidence of submission/acknowledgement, and relevant correspondence is retained in the (TMF).

***For example, where a DSUR contains unblinded information, it is reasonable that copies of the DSUR are not filed in the TMF until the end of the trial when the data has been unblinded. In the event of audit or inspection, the RGO would be able to provide the unblinded reports.**

6.0 Development Record

The table below summarises the revisions introduced in this version. Full historical change records are available within archived SOP versions.

Date	Issue Number	Description Of Changes (If any)
April 2026	6.0	• Language updates in accordance with ICH GCP E6(R3) and UK Clinical Trials Regulations. • Updating wording and processes throughout to improve reading and understanding. • Updated Appendix 1 to match the requirements of the Guidance on Development Safety Update Report (E2F). • Removal of full historical SOP review record; only the latest approved revision is now displayed, with prior versions retained in the document archive