# Pharmacovigilance: Sponsor Overview and Trend Analysis

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| Author: | Camille Bach |
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## 1 Introduction

1.1 The Academic & Clinical Central Office for Research & Development (ACCORD) is a joint office comprising clinical research management staff from NHS Lothian (NHSL) and the University of Edinburgh (UoE).

1.2 This SOP details the process of Sponsor overview and trend analysis of safety reports, for studies sponsored by the UoE and/or NHSL.

## 2 Purpose

2.1 To document the procedure for preparing and submitting Sponsor safety review reports, Development Safety Update Reports (DSURs) and Trial/Data Monitoring Committee (DMC) specific line-listing reports.

## 3 Scope

3.1 This Standard Operating Procedure (SOP) applies to all relevant ACCORD (UoE and NHSL) staff, and at least two nominated, appropriately qualified, independent clinicians ('Independent Assessors').

## 4 Responsibilities

4.1 It is the responsibility of two Independent Assessors to review cumulative safety reports and carry out trend analysis, on a quarterly basis.

4.2 It is the responsibility of the Pharmacovigilance Officer, Pharmacovigilance Manager or designee, to;

- Generate cumulative safety reports, every quarter, from the ACCORD Pharmacovigilance (PhV) databases;

- Follow-up on any actions or queries raised by the Independent Assessors of the safety report;
- Submit DSURs for Clinical Trials of Investigational Products (CTIMPs) to the appropriate Research Ethics Committee (REC) if required and to relevant Competent Authorities;
- Identify and advise Investigators of annual due dates for DSURs;
- Generate line listings for Trial/DMC/DSUR specific reports;
- MedDRA code Serious Adverse Events (SAEs) for DSURs.

4.3 The responsibility for preparation, payment of the MHRA fee and sign-off of the DSUR is delegated to the Chief Investigator (CI) of the trial.

# 5 Procedure

## 5.1 Sponsor Quarterly Review

5.1.1 The Pharmacovigilance Manager, or designee, will generate a quarterly cumulative safety report.

5.1.2 The quarterly cumulative safety report will be comprised of a précis of each relevant study, including the number of participants recruited.

5.1.3 There will also be a cumulative line-listing of SAEs, SARs and SUSARs for all relevant studies. The line listing will summarise safety data from:

- CTIMPs that do not have a DMC but that have reported at least one Serious Adverse Event (SAE)/Serious Adverse Reaction (SAR)/Suspected Unexpected Serious Adverse Reaction (SUSAR);
- CTIMPs, with a DMC, only if the DMC has raised a concern, or if the Sponsor has raised a concern.
- Non-regulated studies where it was decided during Risk Assessment that a quarterly review of SAEs will be needed.

5.1.4 The Pharmacovigilance Manager, or designee, will send the quarterly cumulative safety report by e-mail to two Independent Assessors, for clinical review.

5.1.5 Any follow-up actions or queries raised by the Independent Assessors will be addressed by the Pharmacovigilance Manager, or designee, and reported back to the Independent Assessors. Once the assessors are happy with the report contents, they will undertake a review and trend analysis.

5.1.6 The Independent Assessors will complete the clinical review and trend analysis of the quarterly cumulative safety report within approximately 2 weeks of receipt, and confirm this by e-mailing the Pharmacovigilance Manager, or designee, stating;

- No action required: Reviewed and no issues with the SAEs in the report OR
- Action required:
    - Re-review of study SAEs [as defined by reviewer] Discussion between reviewers.
    - Convene discussion with [Sponsor, CI, PI, Pharmacist, DMC and other relevant people as required].

5.1.7 If trends are identified by the assessors, the Pharmacovigilance Manager, or designee, will take appropriate action, eg. Raise the trend analysis at the next Sponsorship meeting or initiate an Urgent Safety Measure as per SOPs CR005 and CR006. Appropriate action will be decided and documented.

5.1.8 The Pharmacovigilance Manager, or designee, will retain electronic copies of the quarterly cumulative safety reports in the Pharmacovigilance folder on the ACCORD Sharepoint.

### 5.2 Development Safety Update Reports (DSURs)

5.2.1 The Pharmacovigilance Officer, or designee, will;

- Maintain a DSUR tracker in the Pharmacovigilance folder on the ACCORD Sharepoint directory;
- Use the DSUR tracker to identify the annual due dates for DSURs for CTIMPs;

5.2.2 Send DSUR reminders to the CIs by e-mail approximately 6 weeks before the last day of the reporting period (i.e. the Clinical Trial Authorisation (CTA) date). The reminder will also include a mention that the MHRA DSUR fee has to be paid in order for the submission to the MHRA to be possible.

- Generate the SAE line listings and cumulative summary tabulations of SAEs as of the end of the DSUR reporting period, for the DSUR, unless contracted to a third party.

5.2.3 Send a report of line listings and summary tabulations (blinded, as necessary) to the CI for review (if no SAEs have been reported for the study at the end of the DSUR reporting period, an email should still be sent to the CI to inform them about it).

5.2.4 MedDRA code Serious Adverse Events (SAEs) for DSURs as per SOP PV004.

- Instruct the CI that the final report should be returned to ACCORD for submission to the REC if required and competent authority.

5.2.5 The Pharmacovigilance Manager, or designee, will ensure that any unblinded information is inserted into the report only prior to submission to the MHRA or REC and that no unblinded information will be shared with the CI or trial team (i.e. an unblinded report should not be sent to the CI or trial team for review).

5.2.6 Once final content has been agreed, the DSUR will be signed by the CI and returned to the Pharmacovigilance Officer, or designee. The Pharmacovigilance Officer, or designee, will then enter the unblinded information into the DSUR.

5.2.7 The Pharmacovigilance Officer, or designee, will submit the final DSUR report to the Competent Authority(/ies) with a covering letter (.pdf) that includes the name of the study, the EudraCT number or ISRCTN number and reporting period for the DSUR, in addition to any further relevant information. A proof of the DSUR fee payment to MHRA will also be attached if applicable.

5.2.8 For trials that have not gone through the Combined review process:

The Pharmacovigilance Officer, or designee, will;

- upload the .pdf version of the DSUR, proof of the MHRA fee payment and covering letter to the MHRA Submissions Portal. Acknowledgement of receipt will be saved in the SharePoint file with the relevant DSUR and a paper copy will be printed and placed in the TMF/Sponsor file as appropriate.
- follow up with the MHRA if MHRA Submissions Portal acknowledgement is not received.
- submit a final .pdf version of the DSUR report to the appropriate REC(s) by e-mail. All correspondence regarding REC submissions of the DSUR will be filed electronically and hard copies will be placed in the TMF/Sponsor file as appropriate.
- In addition, for UK submissions, a completed Safety Report to a Research Ethics Committee form will be included. Both hard and electronic copies of the UK Safety Report Form, when signed and returned by the REC, will be saved in the safety section of the Sponsor file or TMF, and corresponding electronic folders. The REC can also provide an acknowledgement email receipt instead of a signed Safety Report Form. The email will be uploaded on Sharepoint and a paper copy will be saved in the safety section of the Sponsor file or TMF, and corresponding electronic folders.

- The Pharmacovigilance Officer, or designee, will follow up with the REC(s) if acknowledgement is not received.

5.2.9 For trials that have gone through the Combined review process:
The Pharmacovigilance Officer, or designee, will;

- Upload the .pdf version of the DSUR, proof of the MHRA fee payment and covering letter to the Integrated Research Application System (IRAS) Combined review Portal. Acknowledgement of receipt and other MHRA correspondences will be saved in the SharePoint file with the relevant DSUR and a paper copy will be printed and placed in the TMF/Sponsor file as appropriate. Combined review applications should not submit their DSURs through the MHRA's Medicines Portal. DSURs do not need to be reported separately to the REC.
- If an acknowledgement is not received via email, the Pharmacovigilance Officer will follow-up with the IRAS Help Desk (service.desk@hra.nhs.uk) directly.

5.2.10 The completed and signed DSUR will be printed and saved in the safety section of the appropriate study folder.

5.2.11 Final, unblinded reports must be placed in a sealed tamper-proof envelope and filed in the sponsor file or sponsor held TMF. In case an envelope needs to be opened, the date it is opened (and closed), name, job title and signature of the person responsible for the opening / closing of the envelope should be captured on the envelope. A reason for opening should also be added. The envelope must be re-sealed after each opening. Electronic files that contain unblinded information should be saved in the restricted access "SUSAR" folder (accessible only by the PhV Team and QA) on SharePoint.

5.2.12 Onward reporting to third parties will comply with contractual obligations. The DSUR tracker will be checked for onward reporting requirements. This tracker is maintained by the Pharmacovigilance Officer, or designee and held in the Pharmacovigilance folder on the ACCORD Sharepoint directory.

## 5.3 Trial Specific/DMC Reports

5.3.1 On request (e.g. Trial Manager, CI, Trial Statistician or Research and Development (R&D) Director), the Pharmacovigilance Officer, or designee, will generate line listings for specific trials, (eg. For the DMC) from the ACCORD PhV databases.

5.3.2 The request should specify the reporting period required and give a minimum of 1 weeks' notice for the generation of a trial specific report.

5.3.3 Note that as there may be ongoing follow-up of missing and inconsistent data, any report produced may not reflect the final status of the study safety data.

5.3.4 Trial specific reports will be saved electronically in the safety section of the relevant study folder by the person who generated the report. Where ACCORD holds the Sponsor File, a generic file note will be placed documenting that line listings are stored electronically on SharePoint and a final line listing will be printed and filed at the end of the study. Where ACCORD holds the TMF, line listing filing will be handled on a study specific basis. E.g., if line listings are required for DMC meetings, these should be printed and filed in the TMF. Electronic files that contain unblinded information should be saved in the restricted access "SUSAR" folder (accessible only by the PhV Team and QA) on SharePoint. If any listing that contains unblinded information requires to be printed, it must be placed in a sealed tamper-proof envelope and filed in the sponsor file or sponsor held TMF. Opening of the envelope will follow the process described in point 5.2.8.

5.3.5 For studies with a DMC, the CI or Trial Manager will provide copies of the DMC meeting minutes to ACCORD for review. Any issues will be raised at the regular Sponsorship meeting.

### 5.4 Hosted Studies

5.4.1 Where NHSL is the host of a CTIMP which is externally sponsored, it is the responsibility of the PI to review and retain SAE reports and to raise any issues with NHSL R&D, as the PI believes necessary.

## 6 References and Related Documents

- CR005 Identifying, Recording and Reporting Adverse Events and Urgent Safety Measures for Clinical Trials of Investigational Medicinal Products.
- CR006 Identifying, Recording and Reporting Adverse Events and Urgent Safety measures for non-Clinical Trials of Investigational Medicinal Products.
- CR008 Preparing and Submitting Progress and Safety Reports.
- PV004 Pharmacovigilance: MedDRA Coding SAEs for DSURs.

## 7 Document History

| Version Number | Effective Date | Reason for Change |
|---|---|---|
| 1.0 | 25 AUG 2016 | New SOP. PV001 split. PV002 now captures timetabled reporting. |
| 2.0 | 04 JAN 2019 | Reference to annual safety reports has been removed. Quarterly cumulative safety reports will be generated. Reference to PV004 added. Minor clarifications made throughout. |
| 3.0 | 25 JUN 2021 | Sections 5.2.5 and 5.2.6 updated to remove reference to CESP and replace with the MHRA Submissions Portal |
| 4.0 | 27 JUL 2023 | Update to include PhV Manager and PhV Officer responsibilities.<br>Update following the Combined Review process.<br>Update section 5.1.3 to include non-CTIMPs study when judge necessary during Risk Assessment<br>Update following internal Audit in Nov-2022 to include a clearer process on the blind envelope for paper filing.<br>Section 5.3.4 updated to explain line listing filing process depending on Sponsor file/TMF<br>Sections 5.2.8 and 5.3.4 updated to explain process for storing unblinded DSUR / line listing reports. |
| 5.0 | 12 AUG 2025 | Update to align with new ACCORD branding.<br>Update to mention the MHRA DSUR fee that has to be paid before submission of DSUR.<br>Update of 5.2.5 as it is not mandatory anymore for REC to return a signed Safety Report Form, an acknowledgement email is valid to confirm the DSUR submission to the REC.<br>Minor typo and clarifications updates. |

## 8 Approvals

| Sign | Date |
|---|---|
| Camille Bach<br><br>AUTHOR: Camille Bach, Pharmacovigilance Manager, UoE, ACCORD | 28-Jul-2025 |
| Sweta Rath<br><br>APPROVED: Sweta Rath, Pharmacovigilance Officer, UoE, ACCORD | 28-Jul-2025 |
| L. Mackenzie<br><br>AUTHORISED: Lorn Mackenzie, QA Manager, NHSL, ACCORD | 28-Jul-2025 |

# PV002 Sponsor Overview and Trend Analysis v5.0

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2025-07-28 - 1:15:54 PM GMT+1

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