Pharmacovigilance: Reference Safety Information & Safety Alerts

Document No.:	PV003 v5.0
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Issue Date:	28 JUL 2025
Effective Date:	11 AUG 2025

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 Summaries of Product Characteristics (SPCs) are subject to revision by the marketing authorisation holder in response to new information that comes to light regarding the product. SPCs often contain the Reference Safety Information (RSI) for studies involving drugs with a Marketing Authorisation.

1.3 Clinical Trials of an Investigational Medical Product (CTIMPs), Clinical Investigations of Medical Devices (CIMD) and/or other studies subject to a formal combined risk assessment (SOP GS002 Combined Risk Assessment) without an SPC will have the RSI defined within an Investigator's Brochure (IB).

1.4 The Medicines and Healthcare products Regulatory Agency (MHRA) issue Medicines recall/notifications when new information becomes available.

1.5 For products that do not hold a marketing authorisation the manufacturer is required to provide the Sponsor (NHSL / UoE) with any new information about toxicology or safety data. This requirement will be specified in the applicable agreement with the manufacturer.

2 Purpose

2.1 The purpose of this Standard Operating Procedure (SOP) is to outline the procedures for tracking, and informing trial teams, of updates to the SPC/IB. The SPC/IB include the RSI for the Medicinal Products used within a trial.

2.2 This SOP describes the procedure to be followed on receipt of a Medicines recall/notification from the MHRA or other relevant bodies.

2.3 This SOP also describes the procedure to be followed on receipt of new information regarding safety or toxicology data from manufacturers or relevant bodies.

3 Scope

3.1 This SOP applies to all ACCORD UoE staff involved in the activities described in this SOP.

4 Responsibilities

4.1 It is the responsibility of the Pharmacovigilance (PhV) Officer, or designee, to;

- Maintain an awareness of changes to SPCs/IBs;
- Inform research teams of SPC revisions;
- Ensure IBs are reviewed annually and updated if required;
- Inform research teams of relevant Medicines recall/notifications and maintain the drug safety alert spreadsheet.

4.2 It is the responsibility of the Clinical Research Facilitator or designee to inform the PhV team when an amendment relating to an SPC/IB has been submitted during the Development Safety Update Report (DSUR) reporting period.

5 Procedure

5.1 Tracking

5.1.1 The PhV Officer, or designee, will maintain a tracker of CTIMPs, CIMDs and other studies which have undergone a formal combined risk assessment (GS002) that have an SPC or IB. The tracker will include;

- The date of Clinical Trial Authorisation (CTA), where applicable, from the UK competent authority;
- The name of the Chief Investigator (CI) and other relevant contacts.
- The date and marketing authorisation holder of the SPC (for each Investigational Medicinal Product, active comparator and Non-Investigational Medicinal

Product) that was included in the regulatory submission which led to the CTA being granted. NB: the 'date' of the SPC is taken to be the 'date of revision of the text' (normally provided within section 10 of the SPC document) and NOT the date of publication, or date of upload to the internet, of the document);

- The date, version number and manufacturer/sponsor of the IB (for each Investigational Medicinal Product, active comparator, Non-Investigational Medicinal Product and device) that was included in the regulatory submission which led to the CTA being granted;
- Details of subsequent revisions to the SPC that were notified to the CI;
- Details of which version holds the current approved RSI;
- Date of SPC/IB version checks performed;
- Any other necessary information.

5.2 Updates to SPCs

5.2.1 The PhV Manager or designee, with the help of the Clinical Research Facilitator or designee, will record details of the study SPC in the SPC/IB tracker, held in the Pharmacovigilance (PhV) folder on the ACCORD SharePoint site. This will be done at the time of submission to the MHRA and/or Research Ethics Committee (REC).

5.2.2 Thereafter, on an approximately 6 monthly basis, the PhV Officer, or designee, will ascertain if there have been any updates to the SPC. This information can be obtained from the EMC website, the marketing authorisation holder's website, or the MHRA website. (NB. The frequency of RSI checks will be discussed and documented at the trials risk assessment as per GS002).

5.2.3 Representatives of the sponsor may also receive notification of SPC updates from the holders of manufacturing authorisations. Details of updates will be forwarded to the safety@accord.scot inbox.

5.2.4 If there have been any revisions to the SPC, the PhV Officer, or designee, will ascertain whether the change affects the RSI and will make the new documentation available to the CI for review.

5.2.5 Where the update to the SPC does not constitute an RSI change

5.2.5.1 The PhV Officer, or designee, will inform the CI and/or Trial Manager (TM) that there has been an update to the SPC and make the new documentation available to them for review.

5.2.5.2 A receipt of confirmation of update from the CI and/or TM should be filed electronically in the relevant study folder and also filed in the Trial Master File (TMF)/sponsor file where applicable.

5.2.5.3 The PhV Officer, or designee, will instruct the CI and/or TM to file the revised SPC in their Investigator Site Files (ISFs) but will confirm to the CI/TM that the existing RSI, as contained within the SPC submitted to, and approved by, the relevant competent authority/ies, remains the RSI in use for the study.

5.2.6 Where an update in SPC constitutes a change to the RSI

5.2.6.1 The PhV Officer, or designee, will inform the CI and/or TM that there has been an update to the SPC and make the new documentation available to them for review.

5.2.6.2 A receipt of confirmation of update from the CI and/or TM should be filed electronically, along with any correspondence regarding the change, in the relevant study folder and also filed in the TMF/sponsor file where applicable.

5.2.6.3 The PhV Officer, or designee, will inform the CI and/or TM that although an updated version has been released, they are to refer to the current approved version of the SPC for the RSI until an amendment for the new RSI has been submitted to, and approved by, the relevant competent authority/ies.

5.2.6.4 If not already submitted, the amendment should be submitted and approved in time for the beginning of the next DSUR reporting period. In order to allow for synchronisation of the update of the RSI with the onset of a new DSUR reporting period, investigators should submit amendments that prospectively implement updated RSIs at the start of the next DSUR reporting period.

5.2.6.5 Once an amendment is approved, the Clinical Research Facilitator will notify the PhV Manager, or designee, and the PhV Manager, or designee will update the SPC tracker accordingly.

5.2.6.6 Throughout the trial, the study team can refer to the most recently available version of the SPC (for reasons other than assessing expectedness of Serious Adverse Reactions using the approved RSI).

5.3 Updates to Investigator Brochures (IBs)

5.3.1 The PhV Manager or designee, with the help of the Clinical Research Facilitator, or designee, will record details of the study IB in the SPC/IB tracker, held in the PhV folder on the ACCORD SharePoint site. This will be done at the time of submission to the MHRA and/or REC.

5.3.2 Thereafter annually, and in line with the DSUR due date (where applicable), the PhV Officer, or designee, will contact the CI to ascertain if there have been any updates to the IB.

5.3.3 If the study is not regulated and therefore no DSUR is required, the CI will be contacted on an annual basis from the date of the current approved IB.

5.3.4 The Clinical Research Facilitator will inform the PhV Manager, or designee, when an amendment has been submitted during the DSUR reporting period. The PhV Manager, or designee, will then contact the CI to determine if any changes have been made to the IB that affect the RSI.

5.3.5 If the IB has been updated, the PhV Manager, or designee, will confirm that the CI has filed the revised IB in the ISF and has ensured that all members of the trial team have access to a copy of the revised IB. The SPC/IB tracker will also be updated by the PhV Manager or designee, with the help of the Clinical Research Facilitator, or designee.

5.4 Trial Master File

5.4.1 The PhV Officer, or designee, will ensure that SPC/IB updates are filed in the TMF/sponsor file. If the TMF is held by a designee e.g. a Trial Manager, the revised SPC/IB will be sent to Trial Manager with instructions to file the document in the TMF. If it is agreed, the Trial Manager may distribute the revised SPC or IB to the investigators on behalf of the PhV Officer, or designee.

5.5 MHRA Medicines recall/notifications

5.5.1 Regular Medicines recall/notifications are received from the MHRA by the PhV team, subscribed to this service.

5.5.2 When deemed necessary by the PhV team, a meeting may be convened to discuss actions required as a result of a drug safety update.

5.5.3 The PhV Officer, or designee, will add details of the alert to the Drug Safety Update spread sheet, held in the PhV folder on the ACCORD SharePoint site, and determine which studies, if any, are affected by the alert.

5.5.4 The PhV Officer, or designee, will send an e-mail to the CI/ /Trial Manager of affected studies within five working days of receipt of a medicine recall/notification.

5.5.5 Acknowledgement of CI receipt of this new information will be documented by way of a return e-mail.

5.5.6 Medicines recall/notification correspondence will be saved electronically in the relevant Studies folder and a paper copy filed in the TMF/Sponsor File.

5.6 Manufacturer safety and toxicology data

5.6.1 When new information about safety and/or toxicology data are received by the PhV Team, the PhV Officer, or designee, will send an e-mail to the CI, or designee (e.g.Trial Manager) of the affected studies within five working days of receipt of the information.

5.6.2 The CI will be required to acknowledge receipt of this new information by way of a return e-mail. The CI will consider any safety implications and follow-up with relevant stakeholders if action is required.

5.6.3 Safety/Toxicology data correspondence will be saved electronically in the relevant Studies folder and a paper copy filed in the TMF/Sponsor file.

6 References and Related Documents

- http://www.medicines.org.uk/emc/
- GS002 Combined Risk Assessment

7 Document History

Version Number	Effective Date	Reason for Change
1.0	27 FEB 2017	New SOP.
2.0	22 JAN 2019	The frequency of conducting SPC checks has been changed from monthly to approximately 6 monthly. The frequency of RSI checks will be documented at

		the combined risk assessment (GS002). Other minor clarifications made throughout.
3.0	19 JUN 2020	Clarification of identification of different versions of SPCs by 'date of revision of text'. Affirmation that source of RSI following SPC updates remains the SPC approved by the competent authorities, until such time as the RSI is updated by amendment. Sundry other minor clarifications.
4.0	09 JUN 2023	Change to section 5.4. MHRA have renamed Drug Safety Updates to Medicines recall/notifications. Update to reflect PhV team responsibilities. Change of author.
5.0	11 AUG 2025	SOP updated to align with new ACCORD branding. Update of PhV Officer responsibilities. Update of title and addition of 1.5, 2.3 and 5.6 about manufacturer's safety and toxicology data.

8 Approvals

Sign	Date
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Final Audit Report 2025-07-28

Created:	2025-07-25 (British Summer Time)
By:	Gavin Robertson (v1grobe9@exseed.ed.ac.uk)
Status:	Signed
Transaction ID:	CBJCHBCAABAAK3gGg25CrngOoWmrsTQR0gIhR3iLNP89

"PV003 Pharmacovigilance - RSI and Safety Alerts v5.0" History

Document created by Gavin Robertson (v1grobe9@exseed.ed.ac.uk)
2025-07-25 - 09:49:05 GMT+1- IP address: 90.251.186.46

Document emailed to Camille Bach (Camille.Bach@ed.ac.uk) for signature
2025-07-25 - 09:51:02 GMT+1

Document emailed to Sweta Rath (Sweta.Rath@ed.ac.uk) for signature
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2025-07-25 - 09:51:02 GMT+1

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2025-07-25 - 10:09:59 GMT+1- IP address: 52.102.18.5

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Signature Date: 2025-07-25 - 10:10:22 GMT+1 - Time Source: server- IP address: 62.253.82.243

Email viewed by Camille Bach (Camille.Bach@ed.ac.uk)
2025-07-28 - 07:45:44 GMT+1- IP address: 104.47.11.254

Document e-signed by Camille Bach (Camille.Bach@ed.ac.uk)
Signature Date: 2025-07-28 - 07:46:03 GMT+1 - Time Source: server- IP address: 81.109.241.151

Agreement completed.

2025-07-28 - 07:46:03 GMT+1