

SOP-QA-21 V4

Title: APRs and DSURs	
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Document History

Version	Description of update	Date Effective
1	Change of number for Q-Pulse, Addition of other NHS areas to scope.	2-10-15
2	Reformatted	1-4-17
3	Updated DSUR submission process at 3.8 – 3.18, Abbreviations expanded	1-8-20
4	1.1 & 1.2 – text updated, 3.13 moved to 3.19, 3.15– updated to ICH E2F guidance, Formatting updated	11-10-22

1. Scope

- 1.1 This SOP applies to all researchers involved in research projects sponsored or co-sponsored by University of Aberdeen (UoA) and/or NHS Grampian (NHSG). These studies will have obtained Research Ethics Committee (REC) approval and the SOP describes the procedure for preparing and submitting an Annual Progress Report (APR). APRs are only required for studies that are more than two years in duration and for Research Tissue Bank and Research Databases. There is no requirement for a Progress Report for Proportionate Review studies or where the study is two years or less in duration.
- 1.2 For Clinical Trials of Investigational Medicinal Products (CTIMP), and other interventional studies involving a Medicinal Product (MP), which are sponsored or co-sponsored by University of Aberdeen (UoA) and/or NHS Grampian (NHSG) and which have obtained Clinical Trials Authorisation (CTA). This SOP describes the procedure for preparing and submitting a Development Safety Update Report (DSUR).

2. Responsibilities

Chief Investigator (CI)	Completing and submitting APRs and DSURs (delegated by Sponsor).
Sponsor	Review APRs and DSURs prior to submission.

3. Procedure

Preparation and submission of an Annual Progress Report (APR) to the NHS REC

- 3.1 An APR shall be submitted annually for all research projects with a duration of more than 2 years which have NHS REC approval. The first APR is due 12 months after the date of the favourable opinion for the research project and shall be submitted within 30 days of this date, regardless of whether or not recruitment has started. If recruitment has not started, an explanation shall be included in the APR.

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- 3.2 The APR shall be completed on the appropriate Health Research Authority (HRA) Annual Progress Report Form. The most recent versions can be obtained on the HRA website www.hra.nhs.uk
- 3.3  For non-interventional research projects, the CI shall ensure signed APRs are submitted to the NHS REC which provided the favourable opinion; as hard copy or by email. The APR shall also be copied to the Sponsor and to any NHS R&D departments which have given management permission.
- 3.4 For all interventional research projects, including CTIMPs, other interventional studies involving a Medicinal Product (MP), Medical Device Clinical Investigation (MDCI) and other interventional studies, the CI shall forward the draft APR to the Sponsor for review **at least** 2 weeks prior to the required submission date. The Sponsor shall review the draft APR and either confirm that it can be submitted or request changes and further review.
- 3.5 All progress reports shall be acknowledged in writing by the REC within 30 days of receipt. Should the REC require further information they will write to the CI requesting a response. The CI may be required to attend a meeting of the REC to discuss the progress of the study.
- 3.6  The CI shall ensure that a copy of the APR, acknowledgement and any other communication with REC, Sponsor or R&D are filed in the Trial Master File (TMF) (see SOP-QA-7 – Trial Master File).
- 3.7  Following receipt of the first APR, the Chair of the main REC has the discretion to waive the requirement for further APRs on receipt of a written request from the CI. This may be appropriate where a study has completed recruitment and assessments for the study, but has a long period of follow up with minimal participant involvement.

Preparation and submission of a Development Safety Update Report (DSUR) to MHRA and NHS REC

- 3.8  DSURs are required for all studies which require a CTA. The Sponsor is responsible for submitting DSURs to the Medicines and Healthcare products Regulatory Agency (MHRA) and REC which approved the study. This responsibility along with the preparation of the DSUR is delegated to the CI.
- 3.9  DSURs shall be submitted annually. The first DSUR is due 12 months after the date of the CTA and shall be submitted within 60 days of this date.
- 3.10  If a study has not started before the first anniversary, a DSUR is not required, but the CI must provide a letter to Sponsor explaining why the study has not started which shall be submitted to MHRA and REC.
- 3.11  If a study lasts less than one year, a DSUR shall be submitted with a Declaration of the End of Trial Notification Form.

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- 3.12  In the event of a DSUR submission incorporating more than one research project, the earliest CTA date will be used as the annual submission date. For research projects involving MP which have a **Development International Birth Date (DIBD)**, this date may be used for the DSUR submission. The DSUR shall be submitted regardless of whether or not recruitment has started. If recruitment has not started, an explanation shall be included in the DSUR.
- 3.13 The DSUR shall include:
- A letter listing all EudraCT numbers of trials covered by the DSUR.
 - An analysis of the subjects' safety in the concerned CTIMP(s) with an appraisal of its ongoing risk and benefit.
 - A list of all suspected SAEs (the CI shall remain blinded if a blinded study) and SUSARs.
 - An aggregate summary table of SUSARs.
- 3.14 Details of what to include in a DSUR can be found in the ICH E2F guidance.
- 3.15 Copies of completed exemplars are available on request from the Research Governance Team. The MHRA guidance on completing the DSUR is available as an associated document (see 5).
- 3.16  In preparing the DSUR an annual check shall be made on the Summary of Product Characteristics (SmPC/SPC) and/or the Investigator Brochure (IB) to ensure that the safety profile does not require updating (see SOP-QA-14 – SmPC, IB and IMP Dossier). The date of SmPC/SPC check shall be recorded in the DSUR (section 7.1 of DSUR template (TMP-QA-15)). Any update to the IB should also be recorded in this section. The Reference Safety Information (RSI) used shall be that which was in place at the start of the reporting period.
- 3.17  The CI shall forward the draft DSUR to the Sponsor for review at least 2 weeks prior to the required submission date. The Sponsor shall review the draft DSUR and either confirm that the DSUR may be submitted or request changes and further review. For blinded studies, Sponsor may add unblinded information at this stage; ensuring that the CI remains blinded.
- 3.18  The DSUR must be submitted through the MHRA submission portal, via the Human Medicines option. Select 'Development Safety Update Report' as the Regulatory Activity and 'Original Submission' from the Regulatory sub activity dropdown list. Acknowledgements of receipt for DSUR submissions are generated and emailed to the reporter by MHRA Submissions and a copy of this email should be recorded as evidence of submission in the TMF and copied to Sponsor (researchgovernance@abdn.ac.uk).
- 3.19  The CI shall ensure DSURs are submitted to the NHS REC which provided the favourable opinion. The NHS REC form (CTIMP Safety Report to REC) is available on the HRA website www.hra.nhs.uk and shall be completed and sent with the DSUR. REC shall acknowledge receipt.
- 3.20 The format for the NHS REC submission may be electronic or hard copy depending on which NHS REC provided the favourable opinion. REC should be approached for their preferred format.

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- 3.21  The DSUR shall be copied to any NHS R&D departments who have given management permission.
- 3.22  The CI shall ensure that a copy of the DSUR and any communication with the MHRA, REC, Sponsor or R&D are filed within the Trial Master File (TMF) (see SOP-QA-7 – Trial Master File).
- 3.23 In the event of more than one sponsored or co-sponsored trial involving the same MP, the Research Governance Manager shall liaise with the CIs involved to ensure production of a single DSUR.
- 3.24 For research projects which involve combination/multi-drug therapies it is usual for a single DSUR to be prepared and submitted. However, any exceptions to this (see examples in Appendix 1) shall be discussed with the Research Governance Manager in advance of preparing the first DSUR.

4. Abbreviations and definitions

APR	Annual Progress Report
CESP	Common European Submission Platform
CI	Chief Investigator
CTA	Clinical Trial Authorisation (from MHRA)
CTIMP	Clinical Trial of an Investigational Medicinal Product
DIBD	Development International Birth Date
DSUR	Development Safety Update Report
EudraCT	European Union Drug Regulating Authorities Clinical Trials Database
HRA	Health Research Authority
IB	Investigator Brochure
MDCI	Medical Device Clinical Investigation
MHRA	Medicines and Healthcare products Regulatory Agency
MP	Medicinal Product
R&D	Research and Development (NHS)
REC	Research Ethics Committee
RSI	Reference Safety Information
SAE	Serious Adverse Event
SmPC/SPC	Summary of Product Characteristics
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File

5. Related documentation and references

SOP-QA-7	Trial Master File
SOP-QA-14	SmPC, IB and IMP Dossier
SOP-QA-19	Amendments
TMP-QA-15	DSUR template

Copies of completed exemplar DSURs are available from the Sponsor researchgovernance@abdn.ac.uk

[Frequently asked questions regarding the Development Safety Update Report \(DSUR\)](#)

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6. SOP-QA-21 Appendix 1

Multi-drug therapy used in clinical trial(s)	DSUR
Investigational drug (A) + marketed drug(s) (X, Y, Z).	Either a single DSUR focusing on (A+X+Y+Z) or A single DSUR focusing on (A) including data on the multi-drug therapy.
Two investigational drugs (A) + (B).	Either a single DSUR focusing on (A+B) or Two separate DSURs (A) and (B), each including data on the multi-drug therapy.
Two (or more) marketed drugs as an investigational drug combination (X, Y, Z)	A single DSUR focusing on the multi-drug therapy (X + Y + Z).

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