Title: APRs and DSURs

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Approver: Prof Steve Heys, Head of School

Document History

<table>
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<tr>
<th>Version</th>
<th>Description of update</th>
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| 1       | Change of number for Q-Pulse
Addition of other NHS areas to scope. | 2-10-15        |
| 2       | Reformatted                                     | 1-4-17         |

1. Scope

1.1 This SOP applies to all researchers involved in research projects which are 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).

1.2 This SOP applies to all researchers involved in 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). These studies will have obtained Clinical Trials Authorisation (CTA) and the SOP describes the procedure for preparing and submitting a Development Safety Update Report (DSUR).

1.3 This SOP may also be used by staff from other NHS areas, or organisations, with prior agreement.

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 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 this date, regardless of whether or not recruitment has started. If recruitment has not started, an explanation should be included in the APR.

3.2 The APR shall be completed on the appropriate NRES Annual Progress Report Form. The most recent versions can be obtained on the Health Research Authority (HRA) website [www.hra.nhs.uk](http://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 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 the REC, Sponsor or R&D are filed within 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 CTIMPs, and other interventional studies involving a Medicinal Product (MP) that is also used in a CTIMP, sponsored by UoA and/or NHSG.

3.9 ⚠️ DSURs shall be submitted annually. The first DSUR is due 12 months after the date of the Clinical Trials Authorisation (CTA) and shall be submitted within 60 days of this date.

3.10 ⚠️ In the event of a DSUR submission incorporating more than one research project, the earliest CTA authorisation 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.

3.11 The DSUR shall be submitted using the DSUR template (TMP-QA-15). ⚠️ Heads within this template shall not be deleted; for each heading where information is available, the information shall be presented concisely. Where the CI’s team do not have access to information requested in specific sections (eg manufacturing issues, non-clinical data and marketing status) this shall be recorded as ‘not applicable’.

3.12 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).

3.13 ⚠️ 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 to be updated (see SOP-QA-14 – SmPC, IB and IMP Dossier). The date of SmPC/SPC check should 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.
3.14 ⚠️ 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 can be submitted or request changes and further review.

3.15 The CI shall submit the signed DSUR and any associated documents eg SmPC/SPC, IB, to the MHRA on a CD to: Information Processing Unit, Area 6, MHRA, 151 Buckingham Palace Road, Victoria, London SW1W 9SZ

3.16 ⚠️ This submission shall be made via courier or other signed for delivery service. Copies of the delivery request and proof of delivery shall be held in the TMF and sent to the Sponsor via researchgovernance@abdn.ac.uk The receipt of DSURs will not always be acknowledged by the MHRA; however the CI shall be contacted if there is a need to discuss an issue which arises on MHRA review of the DSUR.

3.17 ⚠️ The CI shall ensure DSURs are submitted to the NHS REC who 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. The REC shall acknowledge receipt of the DSUR.

3.18 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.

3.19 ⚠️ The DSUR shall also be copied to the Sponsor and to any NHS R&D departments who have given management permission.

3.20 ⚠️ The CI shall ensure that a copy of the DSUR, acknowledgement and any other communication with the MHRA, REC, Sponsor or R&D are filed within the Trial Master File (TMF) (see SOP-QA-7 – Trial Master File).

3.21 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 the production of a single report for all concerned trials.

3.22 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

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<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>APR</td>
<td>Annual Progress Report</td>
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<tr>
<td>CTA</td>
<td>Clinical Trial Authorisation (from MHRA)</td>
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<tr>
<td>CTIMP</td>
<td>Clinical Trial of Investigational Medicinal Product</td>
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<td>DIBD</td>
<td>Development International Birth Date</td>
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<tr>
<td>DSUR</td>
<td>Development Safety Update Report</td>
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<td>IB</td>
<td>Investigator Brochure</td>
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<tr>
<td>MHRA</td>
<td>Medicines and Healthcare products Regulatory Agency</td>
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<tr>
<td>MP</td>
<td>Medicinal Product</td>
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<tr>
<td>R&amp;D</td>
<td>Research and Development (NHS)</td>
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<tr>
<td>REC</td>
<td>Research Ethics Committee</td>
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Uncontrolled when printed. Please ensure that you are working on the most up to date version of this SOP.

Key to symbols ⚠️ = Important point to note ⚠️ = Warning
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)

SOP-QA-21 Appendix 1

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