York Foundation Trust R&D Unit
Standard Operating Procedure
R&D/S06

Reporting Requirements During Research Studies

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Unit's website and/or Q-Pulse for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive versions of all R&D Unit SOPs appear online. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the R&D Unit website: www.northyorksresearch.nhs.uk/sops.html and/or Q-Pulse

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	Signature:	Signed copy held by R&D Unit
	Date:	13th July 2017
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	Signature:	Signed copy held by R&D Unit
	Date:	13th July 2017

This SOP will normally be reviewed every 3 years unless changes to the legislation require otherwise

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of significant changes
1.0	12th November 2009	
2.0	21st November 2011	Scheduled review. Inclusion of DSUR. Amended to be applicable to non-CTIMP studies.
3.0	15th July 2013	Removal of references to the North and East Yorkshire Alliance. Change of fax number.
4.0	15th August 2017	Change of title and removal of safety aspects to alternative SOPs as existing title confusing

Contents

1 Introduction, Background and Purpose

Clinical Trials of Investigational Medicinal Products (CTIMPs) are legally regulated by the Medicines for Human Use Act 2004 and regulations made by statutory instrument under that Act. [1] This legal framework imposes a number of reporting requirements in addition to those relating to specific adverse events. These reports must be made to the Medicines and Healthcare Products Regulatory Agency (MHRA) and the Research Ethics Committee that gave the favourable ethical opinion for the study (REC).

For non-CTIMPs there are requirements to report various matters to RECs.

In addition to this external reporting investigators are required to inform R&D Offices responsible for care organisations in which research is conducted of any significant matters relating to the research of which these organisations should be aware. This SOP details how these responsibilities should be discharged.

2 Who Should Use This SOP

This SOP should be used by all staff involved in research studies sponsored or co-sponsored by the Trust and by personnel in the R&D Unit

3 When this SOP Should be Used

This SOP should be used when the Trust is the sponsor or co-sponsor of a research study.

The 'sponsor representative' for the Trust is usually a member of the R&D Unit. .

Recording and reporting of Adverse Events is NOT covered in this SOP. Instead, see the specific SOP referenced in Section 5.

Making amendments and how to temporarily halt a study is NOT covered in this SOP. Instead, see the specific SOP referenced in Section 5.

Urgent Safety Measures is NOT covered in this SOP. Instead, see the specific SOP referenced in Section 5.

4 Procedure(s)

4.1 Development Safety Update Report (DSUR) for CTIMPs only

For all CTIMP studies, sponsors are required to submit a safety report to the MHRA and REC, once a year or on request. Preparation of the DSUR is delegated to the CI but the Sponsor must review and approve the report prior to

[1] The Medicines for Human Use (Clinical Trial) Regulations 2004 and the Medicines for Human Use (Clinical Trial) Amendment Regulations 2006, the Medicines for Human Use (Clinical Trials) Amendment (No.2) Regulations 2006, the Medicines for Human Use (Clinical Trials) and Blood Safety and Quality (Amendment) Regulations 2008, and the Medicines for Human Use (Miscellaneous Amendments) Regulations 2009.

the submission being made. Enough time must be allowed for this when considering the timescales of the submission.

4.1.1 Background to the DSUR

Required from 1st September 2011, this is intended to be a common standard for periodic reporting on drugs under development (including marketed drugs that are under further study) among the International Conference on Harmonisation (ICH) regions.

The DSUR is intended to present a comprehensive annual review and evaluation of pertinent safety information collected during the reporting period by: (1) examining whether the information obtained by the sponsor during the reporting period is in accord with previous knowledge of the investigational drug's safety; (2) describing new safety issues that could have an impact on the protection of clinical trial subjects; (3) summarising the current understanding and management of identified and potential risks; and (4) providing an update on the status of the clinical investigation/development programme and study results.

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. All safety issues discovered during the reporting period should be discussed in the text of the DSUR; however, it should not be used to provide the initial notification of significant new safety information or provide the means by which new safety issues are detected.

4.1.2 Responsibility and timelines for submission of DSUR

Responsibility for preparation and submission of the DSUR within the specified timescales is delegated to the CI. Reports must be provided at yearly intervals for the duration of the trial, from trial authorisation until termination.

The 'Development International Birth Date' (DIBD) determines the start of the annual reporting period for the DSUR. This date is the Sponsor's first authorisation to conduct a clinical trial in any country worldwide. The data lock point of the DSUR should therefore be the last day of the one-year reporting period.

The DSUR must be submitted to all concerned regulatory authorities **no later than 60 calendar days** after the DSUR data lock point.

The due date of the DSUR must be clearly documented in the ISF/TMF.

4.1.3 DSURs for Combination Therapies

In general, a single DSUR should be prepared for clinical trials involving a fixed combination product (i.e. a product consisting of at least two active ingredients in a fixed dose that is administered in a single dosage form). If the sponsor is also conducting clinical trials with individual component(s) of the fixed combination product, separate DSUR(s) should be submitted for each component.

4.1.4 Reference Safety Information

The Investigator's Brochure (IB) in effect at the start of the reporting period is the reference document to determine whether the information received during the reporting period remains consistent with previous knowledge of the investigational drug's safety profile. The IB version number and date must be stated in the DSUR. When an IB is not required for a study, the Summary of Product Characteristics (SmPC) should serve as the reference safety information and version information given similarly.

The IB should contain a discrete section, which is the Reference Safety Information (RSI), allowing the IB to be updated independently of the RSI.

The IB in place at the beginning of the reporting period should be appended to the DSUR, regardless of whether the IB or SmPC was altered during the period of the DSUR. The RSI in place at the beginning of the reporting period should be the reference for the expectedness assessments in the DSUR line listings, regardless of whether the RSI was updated during that reporting period. If the IB or SmPC was updated during the reporting period the current version should also be submitted.

The DSUR should include the date and version number of the IB or SmPC used as the RSI.

4.1.5 Completing the DSUR

The DSUR has a standard format and a template is available (see Section 5). It is necessary to complete ALL sections, leaving no section blank – enter 'no information available' or 'not applicable' where necessary.

In case of a first-in-man trial and subsequent short term metabolism or pharmacokinetic studies the DSUR should be notified within 90 days of the end of trial together with the notification of the end of the trial.

4.1.6 Submitting the DSUR

The CI should ensure that the DSUR is reviewed and approved by the Sponsor Representative in the R&D Unit prior to submission. The CI is responsible for signing and submitting the DSUR to the competent authorities where authorisation has been granted for the clinical trial, within 60 days of the data lock point. The MHRA and HRA websites must be checked for up to date submission requirements prior to the time of DSUR submission. A copy of the submitted DSUR must also be provided to the R&D Unit.

A copy of the signed DSUR must be retained in the ISF/TMF together with evidence of posting where submission may be made by post An acknowledgement should always be requested and followed up if not received. To facilitate acknowledgement it is always good practice to include with any postal submission a stamped addressed return envelope enclosing a card, letter or form to be signed and dated by the receiving party. Where submission is made by email or upload then evidence of this should also be retained.

4.2 Annual Progress Report (APR) (all studies with REC approval)

One year from obtaining REC approval, and annually thereafter, the CI must submit an Annual Progress Report (APR) to the Research Ethics Committee (REC). For guidance on this and to download the required form refer to the HRA

website referenced in Section 5. A copy of the signed APR must be retained in the ISF/TMF together with evidence of posting or email submission (recorded delivery is recommended). An acknowledgement should always be requested and followed up if not received then filed in the ISF.

The CI is responsible for making the submission directly to the REC but a copy should be submitted to the R&D Unit at the same time.

4.3 Quarterly Progress Report (QPR) to Sponsor (all studies)

To ensure adequate sponsor oversight the CI is required to submit regular progress reports to the sponsor. Reports are required quarterly, on 1st January, April, July and October, unless specified otherwise by the R&D Group. The Quarterly Progress Report (QPR) template referenced in Section 5 should be used and the report submitted to the R&D Unit no later than 15 working days after the due date using the instructions on the form.

Quarterly Progress Reports for sponsored CTIMPs will be submitted for review to the R&D Group as a standing agenda item.

4.4 Notification of End of Study (all studies)

The CI must notify the R&D Unit of the end date as soon as a study has ended.

The CI must then submit within 90 days an End of Trial Notification Form available to download from the HRA website. Investigators must ensure that the correct form is used for CTIMP, non-CTIMP or device studies.

Submission must be made to the MHRA, REC and/or HRA as appropriate. Refer to the HRA website for information or seek advice from the R&D Unit.

A copy of the signed completed notification must be retained in the ISF/TMF together with evidence of posting, emailing or uploading. An acknowledgement should always be requested and followed up if not received. This acknowledgement and any other correspondence should be filed in the ISF/TMF.

If a CTIMP is terminated before the date specified in the protocol for its conclusion the CI must notify the R&D Unit immediately and is responsible for notifying the MHRA and the REC as soon as possible and within 15 days of the date of termination by submitting the declaration as described above. This must be undertaken in an expedited fashion.

4.5 End of Study report (all studies)

The CI should send a summary of the final research report to the REC (and MHRA for clinical trials of investigational medicinal products) within 12 months of the end of the study. MHRA (devices) may request a copy of the final report of a clinical investigation of a device. Where the study may be multi-national this is the end of study in all participating countries and not just in the UK.

Final report preparation and submission for CTIMPs is described in R&D/S27.

For non-CTIMPS there is no standard format for the final report. As a minimum, investigators should inform the REC whether the study achieved its objectives, the main findings, and arrangements for publication or dissemination of the research, including any feedback to participants. Final reports should be emailed to the REC.

Copies of all final reports should be submitted to the R&D Unit also. These will be shared with the Trust's R&D Group.

5 Related SOPs and Documents

R&D/S05 Research Related Adverse Event Reporting Procedure for CTIMP studies (Including reporting a Pregnancy)

R&D/S07 Implementing Amendments for Research Studies NOT Sponsored by the Trust

R&D S74 Making Amendments to Trust Sponsored Research Studies

R&D/F21 Developmental Safety Update Report (DSUR) Form

R&D/F22 Quarterly Progress Report Form