North Bristol NHS Trust

Standard Operating Procedure

Periodic Reporting to the Research Ethics Committee and Medicines and Healthcare products Regulatory Agency

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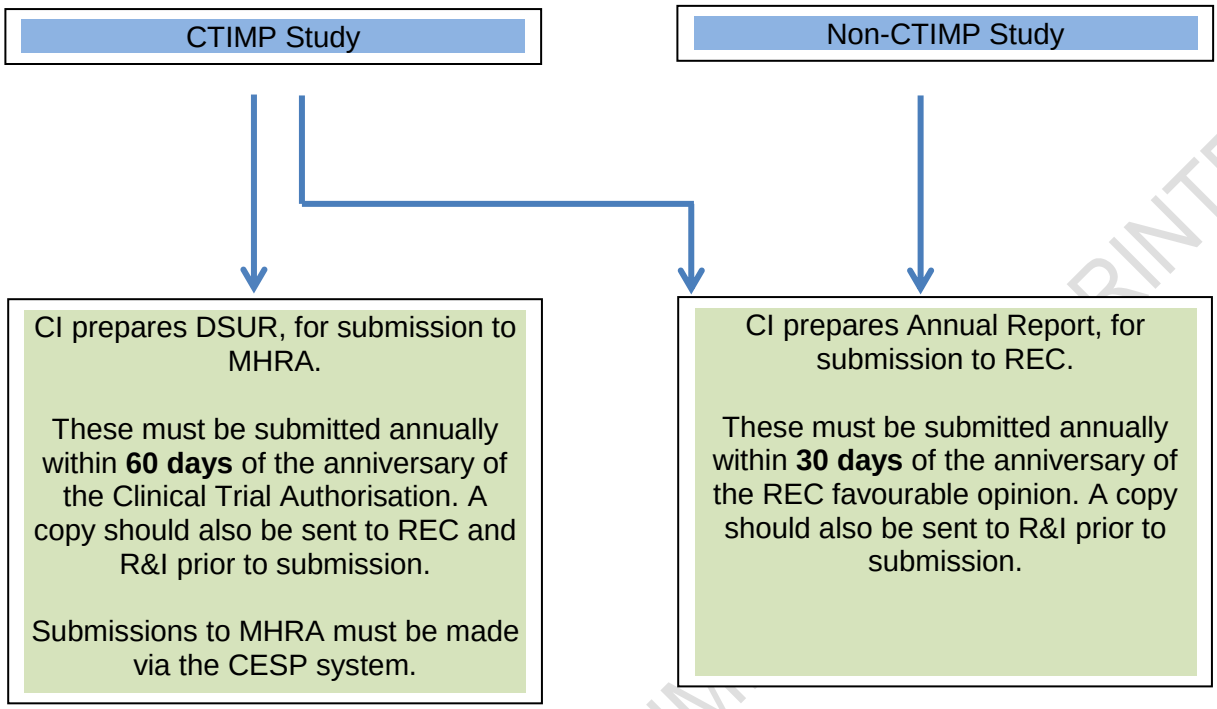
Document Version History

VERSION NUMBER	EFFECTIVE DATE	REASON FOR CHANGE
1.0	01-04-11	To clarify annual safety and progress report responsibilities
2.0	01-03-12	SOP renamed, updated in line with new template and recoded from ISOP-H11
3.0	08-02-16	To clarify that reference safety information must be reviewed at least once a year

DO NOT USE THIS SOP IN PRINTED FORM WITHOUT CHECKING IT IS THE LATEST VERSION

Current versions of all Research & Innovation SOPs and accompanying documents are available online. If you are reading this document in printed form, please check that the version number and date match the most recent version on the Research & Innovation website: www.nbt.nhs.uk/research

i. SOP Flowchart



1. PURPOSE AND SCOPE

The purpose of this SOP is to outline the periodic progress and safety reporting requirements for research studies sponsored by NBT.

After a research study has received all necessary approvals for it to proceed, various bodies and organisations will be interested in its progress. This is particularly the case for CTIMPS which are regarded as high-risk. Annual reports must be reported to REC, and for CTIMPS an annual DSUR must be submitted to MHRA.

The Sponsor is accountable for ensuring periodic reports are submitted within appropriate timelines. Where NBT is the Sponsor, responsibility for compiling and submitting these reports have been delegated to the CI.

2. DEFINITIONS/ABBREVIATIONS

CESP	Common European Submission Portal
CI	Chief Investigator
CTIMP	Clinical trials of Investigational Medicinal Products
DSUR	Development Safety Update Report
HRA	Health Research Authority
NBT	North Bristol NHS Trust
R&I	NBT Research & Innovation Office
REC	Research Ethics Committee
MHRA	Medicines and Healthcare Products Regulatory Agency
NBT	North Bristol NHS Trust
SOP	Standard Operating Procedure
Sponsor	The individual, company, institution or organisation, which takes on ultimate responsibility for the initiation, management (or arranging the initiation and management) of and/or financing (or arranging the financing) for that research

3. WHO SHOULD USE THIS SOP

This SOP applies to all investigators and research team members involved in research studies.

4. WHEN SHOULD THIS SOP BE USED

This SOP is applicable for all studies that are sponsored by NBT.

5. PROCEDURE

5.1. **Responsibilities where NBT acts as Sponsor**

The CI is delegated the responsibility for compiling and submitting periodic reports to NHS REC.

The CI is delegated responsibility for compiling the DSUR for submission by R&I.

For CTIMPs, annual report due dates will be reviewed at trial management meetings between the Sponsor and trial Manager, which are held approximately every two months.

In the event that the CI fails to provide a copy of the reports submitted within the regulatory timeframes, this will constitute a breach of Good Clinical Practice and the procedure will be followed accordingly, see SOP on Managing Breaches of Good Clinical Practice or the Protocol (RI/QMS/SOP/012). Detailed guidance regarding how to prepare and submit reports is outlined in the remainder of this SOP.

5.2. **Periodic Progress Reporting to REC**

REC has a duty to monitor research that has been granted a favourable ethical opinion by it. In order to do so, periodic progress reports are required to be submitted.

Progress reports must be submitted to the REC which granted the favourable opinion. The due date for reports is **12 months** after the date on which the favourable opinion was given and each year thereafter until the end of the trial. The report should be submitted to the Sponsor for approval (CTIMPs) or acknowledgement (non-CTIMP) before being submitted to the REC.

Where a REC regards a trial as particularly high-risk, they may require quarterly or even monthly reports to be submitted. This will be detailed in the approval letter and must be adhered to.

The HRA has produced templates which must be used, available via the HRA website (www.hra.nhs.uk). Separate forms are available for CTIMP and non-CTIMP studies.

Forms should be completed in typescript and signed by the CI. A paper copy should be sent to the REC within **30 days** of the due date, and a copy sent to the R&I.

Once the first progress report has been received by the REC, the chair has discretion to waive the requirement for further reports upon request. This must be agreed in writing by REC and forwarded to R&I. This may be appropriate where a study has completed recruitment and intervention but has a long period of follow-up with minimal participant involvement.

5.3. **Development Safety Update Report (DSURs)**

For CTIMPS, an annual DSUR should be submitted to the MHRA . The DSUR should take into account all new available safety information received during the reporting period. The main objective of a DSUR is to present a comprehensive annual review and evaluation of pertinent safety information collected during the reporting period related to a drug under investigation, whether or not it is marketed.

The DSUR must be compiled annually for the duration of the clinical trial until the regulator has been notified of the end of the trial.

The DSUR due date is the **anniversary** of the first international regulatory approval regardless of the approval status in the UK. The DSUR must be submitted within **60 days** of the due date.

The report should be submitted to the Sponsor for submission 2 weeks before the due date. The data lock point of the DSUR should be the last day of the one-year reporting period.

One DSUR should be submitted for the IMP rather than submitting individual reports for each trial including that IMP. This should occur on the anniversary of the first regulatory approval anywhere in the world and this date is classed as single data lock point. If there is a valid reason for submitting separate reports this should be clearly explained on the DSUR. DSURs are IMP specific therefore for trials involving multi-drug therapy (ie combinations of drugs that are not fixed) R&I, in conjunction with the CI will need to decide to either prepare a DSUR for the multi-drug therapy, or DSURs for one or more of the individual components; in this case information on the multi-drug therapy trials can be included in the DSURs of one or all of the components.

All DSURs must meet the standard that adheres to the European Clinical Trials Directive 2001/20/EC and the Medicines for Human Use (Clinical Trials) Regulations 2004. NBT DSURs should be submitted using the NBT DSUR Template (RI/QMS/SOP/009a), which also includes Guidance for completing the DSUR. Additional guidance is available via the ICH website (www.ich.org).

Submissions to the MHRA must be made via CESP. R&I are the account holder for CESP thus the CI should liaise with R&I. Submissions to REC should be made by email, accompanied by the summary of the DSUR or the CTIMP progress report form available from the HRA website: www.hra.nhs.uk

Please note that the Reference Safety Information (RSI) in the Investigator's Brochure (IB), or Summary of Product Characteristics (SmPC) if used instead, must be reviewed by the CI at least **once a year**. This RSI review should be clearly documented in the Trial Master File. If there are any changes to the RSI, a substantial amendment is required to be submitted to the MHRA and approved before it is implemented in the trial. For further details, see SOP on Safety Reporting: Clinical Trials of Investigational Medicinal Products (CTIMPs) (RI/QMS/SOP/013).

6. DISSEMINATION AND TRAINING

SOPs will be distributed in accordance with the SOP on Preparation of Research SOPs (RI/QMS/SOP/001).

This SOP and any associated templates and forms will be uploaded to the Trust website (www.nbt.nhs.uk/research) and the Managed Learning Environment (MLE) system on the Trust intranet shortly after having been released.

All staff whose activities are subject to this SOP should ensure that they read and understand the content of this SOP.

The training log within the Investigator Site File/Trial Master File should be completed to document that members of staff have read and understood the content of this SOP.

7. RELATED SOPS AND DOCUMENTS

- Health Research Authority (HRA)
  Progress Reports
  www.hra.nhs.uk

- Medicines & Healthcare products Regulatory Agency (MHRA)
  Safety Reporting: SUSARs & ASRs
  www.gov.uk

- The following R&I documents are available on the NBT website: www.nbt.nhs.uk/research

RI/QMS/SOP/009a	DSUR Template
RI/QMS/SOP/012	Managing Breaches of Good Clinical Practice or the Protocol
RI/QMS/SOP/013	Safety Reporting: Clinical Trials of Investigational Medicinal Products (CTIMPs)