STANDARD OPERATING PROCEDURE

SOP 325

STUDY START UP ACTIVITIES FOR CLINICAL RESEARCH TRIALS

Version 1.5	
Version date	27/08/2019
Effective date	27/08/2019
Number of pages	7
Review date	20 April 2020
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Date	21/08/2019
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1 ABBREVIATIONS

CI	Chief Investigator
CRTU	Clinical Research and Trials Unit
CTIMP	Clinical Trial of an Investigational Medicinal Product
GCP	Good Clinical Practice
HRA	Health Research Authority
ICH	International Conference for Harmonisation
IMP	Investigational Medicinal Product
ISF	Investigator site file
MHRA	Medicines and Health Care Products Regulatory Agency
NNUH	Norfolk and Norwich University Hospital
PI	Principal Investigator
R&D	Research and Development
REN	Research and Enterprise Services
SOP	Standard Operating Procedure
TMF	Trial Master File
UEA	University of East Anglia

2 INTRODUCTION

This SOP describes the start-up procedure for a clinical research study.

3 SCOPE

This SOP applies to all healthcare research sponsored by NNUH or UEA which falls within the scope of the Research Governance Framework (2nd edition 2005). Where additional legislation applies - for example the Medicines for Human Use (Clinical Trials) Regulations 2004 (and amendments) or the Medical Devices Regulations 2002 - required procedures will be indicated. External sponsors may require use of their own SOPs and this will be specified in site agreements. It is the responsibility of the local PI to ensure that study specific SOPs can be operated without conflict with this SOP and in accordance with all organisational policies related to research.

4 BACKGROUND

The responsibility for setting up study sites will be delegated by NNUH or UEA as the Sponsor to the CI, and recorded in the Sponsor's Delegation of Responsibility (see SOP 400). In turn, the CI may delegate the responsibility for performing study site set-up activities to an appropriately trained and qualified member of the research team, and this will be recorded in the Study Delegation Log. In the case of CTIMPs or Medical Device trials, the Sponsor will usually be NNUH.

Where the study is adopted by the Norwich Clinical Trials Unit, the Sponsor's Delegation of Responsibility agreed between NNUH, UEA and the Norwich Clinical Trials Unit shall set out the responsibilities for performing study site set-up activities. In turn, the Norwich Clinical Trials Unit may delegate responsibility for some of these activities to the CI and this will be recorded in the Study Delegation Log. This shall be guided by the Norwich CTU Working Practices document on trial management (available from the Norwich Clinical Trials Unit).

5 PROCEDURE

5.1 Approval

5.1.1. It is the responsibility of the Sponsor to ensure that all appropriate approvals have been given and that all agreements are in place before giving written Sponsor approval for the study to commence. In the case of CTIMPs and Medical Device trials, this requires the prior approval of the MHRA (see SOP 405). It is the responsibility of the CI to ensure that no study-specific activities including advertising, screening, discussion with or recruitment of participants, commence before the Sponsor has given approval in writing confirming the approval to proceed with the study.

5.1.2. It is the Sponsor's responsibility to ensure that REC, HRA, Trust R&D and where necessary MHRA approval letters are in place. To support this process, it is the CI's responsibility to ensure that the study has been submitted for review by an external REC, by the HRA and Trust R&D, and for CTIMPs and Medical Device Trials, that the study has also been submitted for approval by MHRA (see SOP 405). It is the CI's responsibility to ensure that all required approvals have been given and that the Sponsor has given written authorisation before recruitment to the study begins.

5.1.3 Any necessary site or other third-party agreements must also be in place before commencement of the study. Examples include: arrangements for handling 24-hour emergency cover; procedures for unblinding; staff absences; IMP management and contracts, arrangements with NNUH Support Departments (e.g. radiology, clinical laboratories), and with all relevant external organisations providing services to the Sponsor as part of the conduct of the study. It is the responsibility of the CI or PI to ensure that appropriate agreement(s) have been reached by the Sponsor. Where NNUH or UEA is the Sponsor, the research support offices (R&D or REN) will put these agreements in place, discussing specifics of the study with the CI and PI as necessary. Where the study involves both UEA and NNUH, the research support offices shall work together to ensure that all appropriate agreements, including those with external organisations, are in place prior to approval and the green light to proceed being given for the study.

5.1.4 For multi-centre studies it is the responsibility of the CI to ensure that all relevant approvals are in place and that the PI at each site has the relevant Site Specific paperwork and any other relevant required approvals before study activities commence. It is the responsibility of the PI to ensure that the Site Specific Agreement, local NHS R&D approval and any other approvals required by the host organisation, are in place before any study specific activities commence at that site.

5.2 Establishing a Trial Master File and Investigator Site File

5.2.1 The CI or designee is responsible for establishing a Trial Master File (TMF) (see SOP 305).

5.2.2 All external sites must establish an Investigator Site File (ISF) (see SOP 305).

5.2.3 It is the responsibility of the CI and PI (s) or designee to ensure that all essential documents are filed in the TMF and/or ISF respectively.

5.2.4 All study related documents, including the TMF and ISF should be stored securely and in a manner that protects confidentiality according to ICH GCP.

5.2.5 The TMF and ISF should be maintained in a ready state to allow for audit, inspection and/or monitoring on request, and that they are subsequently archived appropriately (see SOP 900).

5.3 Other study start-up activities

5.3.1 For CTIMPs, where NNUH or UEA is the Sponsor, the research support offices will ensure that an IMP and Drug Accountability agreement has been reached with NNUH Clinical Trials Pharmacy and that the study is registered with them as per their requirements, discussing specifics of the study with the CI and PI as necessary.

5.3.2 The CI or PI should continue the risk assessment undertaken during proposal/protocol development (SOP 320), considering the appropriate mitigation, management and monitoring strategy for each risk identified (SOP 330). The risks may arise from the protocol and study procedures or from the risks associated with the training and experience of the trial team or host sites. For CTIMPs, the current regulatory framework allows for a range of risk adapted approaches according to how much is known about the medicine(s) being investigated (SOP 320).

5.3.3 The CI or PI should ensure that all trial supplies are in place.

5.3.4 The CI or PI should ensure that all members of the study team are appropriately trained by qualification, previous experience or study specific training. All training must be documented in the training records of each individual. Where NNUH or UEA is the Sponsor there is a requirement that all staff working on the study and named on the Study Delegation Log have undergone GCP training and that they have current certification of this (see SOP 505). It is also the expectation of NNUH and UEA that this obligation also applies in cases where there is an external Sponsor even if that Sponsor does not otherwise require this.

5.3.5 The CI or PI should ensure that all members of the study team are appropriately trained in pertinent SOPs and NNUH nursing, CRTU, laboratory

and radiological working practice documents, and/or external Sponsor SOPs as appropriate. All training must be documented in the training records of each individual (see SOP 505).

5.3.6 Study Delegation Log

The CI or PI should ensure that the names of all members of the research study team, including the CI or PI, are listed in a Study Delegation Log with a definition of their individual study responsibilities (see SOP 305). The Study Delegation Log must be signed by all members of the research study team and each entry must then be counter-signed by CI or PI. The Study Delegation Log should be kept up-to-date and retained in the TMF or ISF.

6 REFERENCES

- EU Clinical Trials Directive 2001/20/EC
- WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI Ethical principles for Medical Research Involving human Subjects.
- Description of the Medicines for Human Use (Clinical Trials) Regulations 2004

7 RELATED DOCUMENTS

SOP 305: Creating and Maintaining a Trial Master File
SOP 320: Developing a Research Protocol
SOP 330: Monitoring Clinical Trials
SOP 400: Authorisation of Sponsorship
SOP 405: Obtaining MHRA approval for a clinical trial
SOP 505: Creating and Maintaining Training Records
SOP 900: Storage and Retention of Research Documents

Norwich CTU Working Practices document on trial management (available from the Norwich Clinical Trials Unit)

8 APPENDICES

Appendix 1: Change Control, Revision and Review Sheet

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Revision Form: SOP 325				
Version No	Change Date	Reason for Change	Reviewer	Signature and Date
1.1	01/10/2010	Updated to reflect UEA/NNUH joint working arrangements		
1.2	01/07/2013	Updated to include a paragraph on risk assessment and associated references.		
1.3	01/01/2014	To correct spelling or numbering mistakes in previous version, minor alterations to text and combining control and revision sheets	**Debbie Kelly - Research Manager RSC**	***D A Kelly 16th December 2013***
1.4	29/12/2016	Mention of "HRA" in abbreviations. Change to point 5.1.3 to reflect that authorizations have to be in place prior to Commencement of the study rather than prior to submission to REC.	**Julie Dawson - Acting Research Services Manager**	**Julie Dawson** (authorised by email) **29.12.2016**
1.5	14/08/2019	Extension of review deadline 12 month from existing review date, no content changes made.	**Francesca Dockerty – Clinical Trial Monitor NNUH**	**Francesca Dockerty** ***08/08/2019***