Nottingham University Hospitals NHS
NHS Trust

STANDARD OPERATING PROCEDURE

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1. Document History

Version Number	Issue Date	Reason for Change
1	3rd March 2014	Original SOP. It replaces SOP-44.

2. Introduction

This standard operating procedure (SOP) provides guidance on the contracts process and insurance and indemnity demands for Nottingham University Hospitals NHS Trust (NUH) clinical studies.

3. Purpose and Scope

All clinical studies being undertaken at NUH must be governed by a contract and each person working on the study should be contractually bound to NUH. These contracts must be fully characterised or signed and dated by all parties before a clinical study begins. This SOP describes the steps to be followed by all NUH staff.

4. Responsibilities

Everyone who participates in clinical studies at NUH must have a contract with NUH. It is the individual's responsibility to make sure the correct contract with NUH has been established.

Research & Innovation (R&I)
Identify the contracts required for a clinical study and authorise their initiation.

Research Project Manager (RPM)
Identify contracts, offer standard contract advice, issue standard agreements and maintain internal records.

Research Contracts Manager (RCM)
Provide contract/legal advice, review, negotiate and draft non-standard agreements and maintain the contracts archive.

Deputy Director of Research and Innovation
Contractual sign-off.

5. Definitions

CI	Chief Investigator
CMD	Clinical Investigation of a Medical Device
CNST	Clinical Negligence Scheme for Trusts
CRO	Contract Research Organisation
CTIMP	Clinical Trial of Investigational Medicinal Product
Documas	A document management system to assist with the management, control and governance of the research and ethics processes covering research and development projects
Funding Agreement	The contract agreeing financial resource for the clinical study
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
ICH	International Conference on Harmonisation
Indemnity	The guarantee to be responsible for someone else's loss
IP	Intellectual Property
IMP	Investigational Medicinal Product
mCIA	Model Clinical Investigation Agreement
mCTA	Model Clinical Trial Agreement
mNCA	Model Non-Commercial Agreement
NHS	National Health Service
NUH	Nottingham University Hospitals NHS Trust
PI	Principal Investigator
REC	Research Ethics Committee
R&I	Research and Innovation
R&I Approval	Approval issued by NUH R&I for the study to go ahead on NUH premises
RCM	Research Contracts Manager
RPM	Research Project Manager
SOP	Standard Operating Procedure
UKCRC	UK Clinical Research Collaboration

6. Procedure

6.1 Identifying Contracts for a Clinical Study

The R&I department will help to identify the contracts required to conduct the clinical study.

For a clinical study to go ahead, financial funding will be required either from a commercial or non-commercial source. A Funding Agreement must be in place before any other contracts are initiated. Non-commercial funding from the Government is often provided under a standard agreement but commercial funding can be more varied.

The Sponsor of the study will undertake responsibility for the conduct, safety, results and publication which needs to be contractually accounted for. The following are examples of required contracts:

- All staff working on a clinical study at NUH must have a contractual link with NUH. In the majority of cases, this will be via an employment or honorary contract but where those persons are employed by an outside institution or commercial company, a separate contract must be agreed. Contracts with individuals themselves should be avoided; the contract should be signed by their employer. Specific roles, such as the Chief Investigator (CI) or Principal Investigator (PI) of a clinical study will have individual responsibilities such as delivering an acceptable standard of clinical care in accordance with the protocol, monitoring and reporting. These individual responsibilities must be documented and the CI/PI should sign their acknowledgement.
- Investigational Medical Product (IMP), devices and equipment must have a contractual link with NUH. Evidence is obtained (accreditation or an inspection) as to the provider's competence and most importantly, the contract ensures that materials are manufactured/supplied in accordance with Good Manufacturing Practice (GMP) requirements.

- The clinical study may require services from different departments/ institutions or commercial entities, for example Pharmacy, Radiology or PET Scanning. To ensure the study runs efficiently and achieves its milestones and deliverables, a contract with NUH should be agreed. This ensures each service provider is clear on their responsibilities and commits to achieve the required work, standard and timescales.
- Each site will require separate agreements if the study is taking place across a number of different locations. It's the Sponsor's responsibility to ensure all sites have a contract.
- If a non-commercial clinical study involves the transfer of human tissue in or out of NUH then a Material Transfer Agreement (TAFR00408) may be required, governed by the Human Tissue Act 2004. The Material Transfer Agreement considers the person's consent and ensures tissue is only transferred in accordance with their consent to approved persons.
- A Material Transfer Agreement is additionally used for transferring data outside of NUH to external source. The R&I department will advise when a Material Transfer Agreement or a Confidentiality Agreement (TAFR00407) should be used.

6.2 Contracts Process

- The CI will request an initial review meeting with R&I to discuss the contract requirements. Establishing the contracts required may also be done on an individual basis by an RPM or RCM. The RPM will send out the standard agreements or approach the RCM for a bespoke draft. The wording in standard contracts has been pre-approved and does not require additional legal review.
- Any non-standard terms must be submitted to ResearchContracts@nuh.nhs.uk. The standard templates must be used wherever possible, to reduce demand on the R&I department and help the study run efficiently.
- Once the relevant parties have been consulted and the terms of the contract approved, the RPM or RCM will submit the contract for signature. Each party to the contract must sign and date the contract and a copy must be returned to R&I.
- R&I contracts must be signed by one of the following signatories **only**:
    i. Chief Executive
    ii. Director of Research & Innovation
    iii. Deputy Director of Research & Innovation
- The fully signed contract will be filed in the study folder and on the internal research management platform, Documas.
- When all contracts are fully executed, the study can begin.

6.3 Structure and Content

Each study should have the following matters contractually accounted for:

i. Definitions
ii. Obligations of the parties including sponsorship
iii. Regulatory compliance
iv. Reporting of serious adverse events
v. Publication and publicity
vi. Insurance, liability and indemnity
vii. Confidentiality, data protection and freedom of information
viii. Intellectual property rights and ownership of results
ix. Agreement, modification and termination
x. Notices
xi. Dispute resolution
xii. Governing law
xiii. Medical equipment appendix (where appropriate)
xiv. Financial arrangements
xv. Start and end date of the contractual obligations
xvi. Performance monitoring and oversight

6.4 National Health Service (NHS) Indemnity

NUH has an ethical and legal obligation to provide indemnity through The Medicines for Human Use (Clinical Trials) Regulations 2004, the Research Governance Framework for Health and Social Care 2nd Ed. 2005 and the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. It will usually be the Sponsor who makes these arrangements although the responsibility remains with NUH. All clinical studies conducted within NUH must have a nominated Sponsor, whether this is NUH or an external organisation/commercial entity.

A robust process of review and authorisation must be followed before any clinical study can be carried out. The 'R&I Approval' permits the study to be carried out on NUH premises and applies cover of the Clinical Negligence Scheme for Trusts (CNST). The CNST outlines NHS Indemnity, the guarantee by NUH to be responsible for someone else's loss. If a subject in clinical study suffers loss through negligence of NHS staff, that subject will be financially compensated.

The study must have R&I approval for the CNST to apply. The R&I department provide guidance on how to obtain R&I Approval and advise on NUH liability and cover of the CNST.

6.5 Insurance

In accordance with Statutory Instrument 2004/1031 Part 2 Schedule 1, the Sponsor, CI and other relevant parties must ensure that insurance and indemnity provisions for the duration of the study are in place to cover the liability of Sponsor and Investigator. It is important that the Sponsor takes the exclusion criteria into account when determining the insurance cover.

In addition to R&I approval, a clinical study will require approval or favourable opinion by a Research Ethics Committee (REC). If NUH are Sponsor, REC considers whether NHS Indemnity by the CNST is adequate. If not, it may refuse approval and request a non-NHS organisation to Sponsor or give conditional approval/favourable opinion upon evidence of separate insurance being purchased. The NHS cannot purchase commercial insurance so this must be acquired by a commercial entity or non-NHS organisation e.g. a university.

Where a non-NHS organisation is Sponsor, they will not receive cover of the CNST and must provide evidence of a valid insurance policy instead. The cover should be adequate for the study in question and a copy of the relevant clinical trials insurance certificate and policy with exclusion criteria should be provided to NUH.

If the clinical study uses a licensed drug or equipment then the manufacturer must retain product liability and warrant the drug/equipment is fit for purpose. If unlicensed, the drug/equipment may also be subject to safety and functionality testing prior to release for use in the study.

If the clinical study uses a licensed drug/equipment outside the remit of the license then it may also be subject to safety and functionality testing prior to release for use in the study.

6.6 National Research Contract Templates

Use of standard agreements reduces pressure on R&I resource, improves efficiency and ensures important matters are contractually accounted for. NUH use the UK Clinical Research Collaboration (UKCRC) suite of standard agreements for use in studies without modification. NUH seeks to utilise UKCRC standard agreements wherever possible, listed below:

- **mNCA** (model Non-Commercial Agreement) – Studies sponsored by a non-commercial organisation e.g. NHS hospitals;
- **mCTA** (model Clinical Trial Agreement) **–** Commercially sponsored studies;
- **CRO mCTA** – If the management of the clinical study is outsourced to a contract research organisation (CRO), the CRO mCTA provides a template tripartite agreement between the CRO, a commercial sponsor and the NHS organisation where the study takes place;

- **mCIA** (model Clinical Investigation Agreement) – Should be used where a medical device is being tested in NHS hospitals but sponsored by a commercial entity;
- **CRO mCIA** – A tripartite agreement between the CRO, the commercial sponsor of the medical device and the NHS organisation where the research is taking place;
- **Primary Care mCTA** – Should be used for a commercially sponsored trial taking place in NHS primary care; and
- **mICRA** (model Industry Collaborative Research Agreement) – For use in research collaborations between different institutions like commercial entities, NHS organisations and academia across the UK.

As all regulatory inspections are now risk-based, performance monitoring and oversight should be included in all clinical trial-related contracts, no matter which type.

6.7 NUH Templates

The national templates do not provide for all research contract scenarios therefore NUH has devised a group of internal templates which the R&I department will issue, as and when required. As described in section 6.2, the contracts required for each study will be identified by the R&I department in an Initial Review Meeting or on the individual advice of an RPM or RCM. NUH staff outside R&I are not expected to know which NUH templates should apply and cannot directly access the templates. An introduction to NUH research contract templates is provided below:

- **Bipartite Agreement –** This agreement has two parties, NUH and the Chief Investigator of the clinical study. Its purpose is to clearly identify and delegate responsibilities of NUH as Sponsor and the Chief Investigator. There are three types of Bipartite Agreements: 'CTIMP' (TAFR00409); 'CMD' (TAFR00410); and 'Other' (TAFR00411). R&I will advise which is applicable and arrange signature by an authorised signatory of R&I. The Chief Investigator will sign personally in acknowledgement of their documented responsibilities.
- **Tripartite Agreement** – This agreement will be used where NUH is Sponsor and a Third Party has been appointed to manage the study, or specific study activities. There will be three parties: NUH; the Third Party; and the Chief Investigator. The Tripartite Agreement clearly defines responsibilities between the three parties and each is required to sign in acceptance or acknowledgement. Similar to the Bipartite, there are three types of Tripartite Agreement: 'CTIMP' (TAFR00412); 'CMD' (TAFR00413); and 'Other' (TAFR00414). R&I will advise which is required and obtain signature on behalf of NUH as Sponsor.
- **External consultants, goods and services** – These can be contracted via the RCM's using the NUH Consultancy Agreement (TAFR00415) or Services Agreements. An RCM will be required to tailor the template to the specifics of each study. R&I will advise where this is necessary and provide contact with an RCM.
- **Collaboration Agreements –** If NUH is sponsoring a study that requires the participation of other NHS organisations or external institutions like universities, NUH has a template Collaboration Agreement that can be used to agree how the parties will operate. An RCM will be required to tailor the template to the specifics of each study. R&I will advise where this is necessary and provide contact with an RCM.
- **Non-commercial Collaboration Agreement with the University of Nottingham (TAFR00423) –** This template has been agreed with the University of Nottingham and is used to subcontract part of a non-commercial study. For example, where NUH is Sponsor of a study but require a member of University of Nottingham staff to be Chief Investigator. An RCM will draft this as and when required.
- **Shared Care Agreement (TAFR00422) –** Used when study subjects receive treatment by NUH and another hospital/clinic/treatment centre for the same study. This agreement will define the responsibility of each party towards the subject's care. An RCM will be required to tailor the template to the specifics of each study.
- **Commercial Trial Subcontract Agreement with the University of Nottingham (TAFR00424) –** Similar to the above, there is an agreed template with the University of Nottingham for commercial studies. If NUH wish to engage the services of a University of Nottingham employee, this template will be used. R&I will advise when required and a RCM will draft this.

- **InHealth Research Support Services Agreement (TAFR00417)** – Used by NUH as Sponsor, to engage the services of PET Scanning for a study. R&I will advise when required and an RCM will draft this.
- **InHealth PET Scanning Agreement – Trust & Trust (TAFR00418) –** Used when PET Scanning is required for a study but NUH is not the Sponsor. This agreement is made between the Sponsor and NUH. An RCM will draft this.

7. References and Associated Documents

Human Tissue Act 2004
Data Protection Act 1998
The Medicines for Human Use (Clinical Trials) Regulations 2004
Statutory Instrument 2004/1031 Part 2 Schedule 1
Research Governance Framework for Health and Social Care 2nd Ed. 2005
ICH-GCP Guidelines.

Available from the UKCRC website	Agreement Templates
TAFR00407	Confidentiality Agreement
TAFR00408	Material Transfer Agreement
TAFR00409	Bipartite - NUH Sponsor and CI Agreement (CTIMP)
TAFR00410	Bipartite - NUH Sponsor and CI Agreement (CMD)
TAFR00411	Bipartite - NUH Sponsor and CI Agreement (OTHER)
TAFR00412	Tripartite - NUH Sponsor, CI and Third Party Agreement– (CTIMP)
TAFR00413	Tripartite - NUH Sponsor, CI and Third Party Agreement (CMD)
TAFR00414	Tripartite - NUH Sponsor, CI and Third Party Agreement (OTHER)
TAFR00415	Consultancy Agreement
TAFR00417	InHealth Research Support Services Agreement
TAFR00418	InHealth PET Scanning Agreement –Trust & Trust
TAFR00422	Shared Care Agreement
TAFR00423	Non-commercial Collaboration Agreement with the University of Nottingham
TAFR00424	Commercial Trial Subcontract Agreement with the University of Nottingham