STANDARD OPERATING PROCEDURE

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The definitive versions of all UHPNT RD&I Dept SOPs appear online, not in printed form, to ensure that up to date versions are used. 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 Trust's website: https://www.plymouthhospitals.nhs.uk/research-sops

Clinical Trial Agreements (CTA) and Clinical Investigation Agreements (CIA) for commercially sponsored clinical trials

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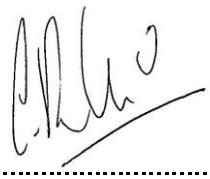
Signature: 

Date: 18th Jan 2019

1 Purpose and Scope

This SOP outlines the procedures regarding execution of a contract for commercially sponsored research studies conducted within University Hospitals Plymouth NHS Trust (UHPNT).

All commercially sponsored research carried out at UHPNT must have a fully executed contract in place before the study starts. This agreement must define the scope of work, establish acceptable payment arrangements, and address important issues including the right to publish research results, protection of confidential information, and indemnification of third parties and/or case injury.

Model Clinical Trial Agreements

In 2006 the Department of Health (DH) and the Association of the British Pharmaceutical Industry (ABPI) published a nationally agreed model Clinical Trials Agreement (mCTA) as a standard contractual framework for commercially sponsored clinical trials involving NHS patients. This agreement is a two way agreement between the NHS Trust and the Commercial Sponsor.

In addition to the above bipartite mCTA for use by NHS Trusts and pharmaceutical companies, a tripartite Contract Research Organisation (CRO) mCTA was published in 2007. Based on the bipartite agreement, it provides a contract model for use when the management a commercially sponsored clinical trial is outsourced by the sponsor to a Contract Research Organisation (CRO).

Model Clinical Investigation Agreements

In 2008 the Department of Health in partnership with the NHS, the Association of British Healthcare Industries (ABHI) and the UK Health Departments published the model Clinical Investigation Agreement (mCIA) as a standard contractual framework for commercially sponsored clinical device investigations involving NHS patients. This agreement is a two way agreement between the NHS Trust and the Commercial Sponsor.

In addition to the above bipartite mCIA for use by NHS Trusts and medical device companies, a tripartite Contract Research Organisation (CRO) mCIA was published in 2009. Based on the bipartite agreement, it provides a contract model for use when the management of a commercially sponsored clinical investigation is outsourced by the sponsor to a Contract Research Organisation (CRO). The above templates can be down loaded from the following link: http://www.ukcrc.org/regulation-governance/model-agreements/mcta/

The appropriate DH/ABPI/ABHI model agreement should be used in all commercially sponsored studies that are conducted within University Hospitals Plymouth NHS Trust

The Research Department is responsible for negotiating and executing CTAs and CIAs at UHPNT; individual investigators may not contractually bind the Trust.

In scope: Commercial research hosted by UHPNT.

Definitions

ABHI	Association of British Healthcare Industries
ABPI	Association of the British Pharmaceutical Industry
CI	Chief Investigator
CIA	Clinical Investigation Agreement
CRO	Contract Research Organisation
CTA	Clinical Trials Agreement
CTIMP	Clinical Trial of an Investigational Medicinal Product
DH	Department of Health
GCP	Good Clinical Practice
HRA	Health Research Authority
ICT	Industry Costing Template
mCIA	model Clinical Investigation Agreement
mCTA	model Clinical Trials Agreement
MHRA	Medicines and Healthcare products Regulatory Agency
NIHR	National Institute for Health Research
UHPNT	University Hospitals Plymouth NHS Trust
RD&I	Research Development & Innovation
REC	Research Ethics Committee
RO	Research Office
SOP	Standard Operating Procedure

2 Who should read this document?

Trust RD&I Manager, Deputy RD&I Manager, Principal Investigator (PI), RD&I Finance Coordinator, RD&I Deputy Finance Coordinator and RD&I Finance Administrator.

3 Procedure to Follow

3.1. Receipt & Initial review

The RD&I Finance Co-ordinator receives a copy of the final study protocol, draft Industry Costing Template and draft CTA/CIA from the commercial company or clinical research organisation (CRO).

Review and agreement of the main body and non-financial appendices of the agreement

The RD&I Manager or Deputy confirms that the agreement provided by the company is accepted. The *aide memoir* maybe utilised for checking Commercial Agreements (Appendix 1) and the model CTA/CIA templates. The standard default is the appropriate DH/ABPI mCTA and its use should be encouraged. If the commercial company insists on using a modified or non-model CTA/CIA the RD&I Finance Co-ordinator will advise that reviewed by Trust solicitors may be required and the cost will need to be paid by the company.

The RD&I Finance Co-ordinator provides feedback to the Company. If there are any areas of disagreement which the RD&I Finance Co-ordinator is unable to resolve, further assistance should be sought from the RD&I Manager and/or Legal advice if required.

The Research Co-ordinator will ensure that within the approved agreement the:

- Trust address is correct
- study and PI details are correct
- level of compensation is appropriate
- target recruitment number is accurate
- Trust notices contact information is correct

3.2 Review of the Industry Costing Template and agreement of the financial appendix

The NIHR Industry Costing Template (ICT) tariffs are used for all set-up fees, investigations and procedures with local variations applied where local time or cost variations are demonstrable.

A review of the ICT (sense check and addition of standard local variations) is performed by the RD&I Finance Co-ordinator or delegate.

The RD&I Finance Co-ordinator reviews the local variations with the sponsor representative. Research nurse team leaders may be approached for discussion on

study procedure timings if required. Trust Support services may also be approached for individual costs as required.

The revised local budget is transposed into the Financial Appendix of the model Clinical Trials/Investigation Agreement (mCTA/mCIA) by the sponsor representative

A full financial review of the ICT and mCTA/mCIA Financial Appendix is performed by the RD&I Finance Co-ordinator. Where required, any further changes are negotiated with the sponsor representative by the RD&I Finance Co-ordinator.

3. Finalisation and signature

Once the main body and all appendices of the CTA/CIA have been agreed, the RD&I Finance Co-ordinator requests that the sponsor representative finalise the agreement and initiate the signature process.

The RD&I Finance Co-ordinator undertakes a final check of the hard copy partially executed CTA and passes to RD&I Manager to authorise prior to signature of the CTA/CIA by the Trust approved signatory (the Associate Director of Finance).

The RD&I Finance Co-ordinator returns two copies of the fully executed CTA/CIA to the Contract Research Organisation (CRO), one copy only to the Sponsor if no CRO involved, a copy to the UHPNT PI for the Investigator Site File and a final copy is retained in the RD&I Master File.

The RD&I Secretary saves a scanned copy of the fully executed CTA/CIA to the study file on the RD&I drive.

4. Authorisation

On receipt of the authorisation notification the RD&I Finance Administrator initiates set-up of invoicing and income distribution processes, including financial side letters with other instructions where applicable.

4 Document Ratification Process

The review period for this document is set as ***default of three*** years from the date it was last ratified, or earlier if developments within or external to the Trust indicate the need for a significant revision to the procedures described.

This document will be approved by the ***RD&I Manager or their Deputy***.

Non-significant amendments to this document may be made, under delegated authority from ***a senior RD&I manager***, by the nominated author. These must be ratified by ***a Senior RD&I manager***.

Significant reviews and revisions to this document will include a consultation with ***appropriately knowledgeable staff***. For non-significant amendments, informal consultation will be restricted to ***staff*** who are directly affected by the proposed changes.

Dissemination and implementation

4.1. Dissemination of this SOP

4.1.1. New SOPs and new versions of existing SOPs: The Research Governance Manager will be responsible for ensuring authorised SOPs are uploaded on the RD&I internet site. Internal Trust Staff are expected to use the RD&I internet site to access latest versions of SOPs and to check the website regularly for updates.

Notice of new or amended procedural documents that have undergone a major amendment will be given *via* the following routes:

- Inclusion in the Trust weekly e-bulletin Vital Signs
- Direct email to Trust Researchers and or teams

4.2. Training in this SOP

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

5 Reference material

Guidance for the model Clinical Trial Agreement for Pharmaceutical and Biopharmaceutical Industry sponsored research in NHS Hospitals (mCTA, 2011 version) http://www.ukcrc.org/wp-content/uploads/2014/03/mCTA-Guidance-2011.pdf

UK Clinical Research Collaboration (UKCRC) - Model Agreements http://www.ukcrc.org/regulation-governance/model-agreements/mcta/

Appendix: Aide memoir- Commercial Agreement checklist — Appendix 1

mCTA section #	Item	Essential items to confirm	Additional issues to consider	Okay? Yes/No
Front page	Agreement	Address should be: University Hospitals Plymouth NHS Trust, Derriford Hospital, Plymouth. Devon PL6 8DH		
Front page	Recitals (whereas…)		Used primarily for scene setting and have limited legal effect. Check that wording makes sense for type of project to be undertaken. Check the title matches the protocol.	
1	Definitions		Ensure that any items defined in this section are capitalised throughout rest of document.	
2.1	Site Principal Investigator obligations	If changed from the model text, the investigator should confirm that they understand and are able to comply. For this purpose, appendix 6 should be sent to PI for confirmation before CTA signature		
2.3	Site Principal Investigator obligations		Trust has responsibility to find PI replacement.	
3.6	Clinical trial Governance	The protocol takes precedence over the CTA. Review for inconsistencies between the protocol and CTA. Onus is on the Trust to ensure that study does not contravene governance		
4.6	Obligations of the Parties			

mCTA section #	Item	Essential items to confirm	Additional issues to consider	Okay? Yes/No
5.6	Liabilities and indemnities		For information, Sponsor indemnity also covers “subcontractors” e.g. if central labs are used they are covered by Sponsor indemnity and you do not need to obtain evidence of separate indemnity for them.	
5.7	Liabilities and indemnities	£5 million cover as minimum. Cover in $ or € of equivalent value is acceptable. A current insurance certificate from an insurance company should be made available to cover the amount specified.	If the level of cover is below the standard level the Research Coordinator should consider level of risk and cover requirements on case by case basis. For example, a questionnaire study or non-interventional observational study would be low risk where as a drug study would be high risk. The Research Coordinator should discuss case with the RD&I Manager and if in any doubt Legal advice should be sought. Self-insurance cover by the commercial company itself is felt to be too risky so CTA offering only this cover should not be signed.	
6.1	Data protection	Check protocol to ensure that it does not contravene Data Protection Act	If transfer of personal data is to take place to non-EU countries Sponsor should ensure that provide an “adequate” level of privacy protection. US companies should confirm they qualify for Safe Harbour Principles (companies may have statement on data protection/Safe Harbour Principles on their company website). ADD ‘and in line with Confidentiality: NHS Code of Practice Nov 2003’	

mCTA section #	Item	Essential items to confirm	Additional issues to consider	Okay? Yes/No
7	Publicity			
8	Publication rights		The Sponsor has the right to "approve" publications, a period of up to 60 days is generally acceptable. Check that the PI accepts cases where period is extended.	
9	IPR		IP is owned by Sponsor. Consider whether Trust may want to use IP resulting from trial during normal patient care– if likely you may want to ask Sponsor for licence without payment.	
10	Financial arrangements	The financial appendix must be reviewed and approved by Research Finance before the CTA is signed.		
11	Term		No definitions given of start and end of the Clinical Trial. Obligations of Parties continue until study ends; therefore may want to clarify what constitutes “end of study”.	
12	Termination clauses	A replacement must be found within 3 months if the current PI is not available for greater than this period.	Be aware that all expenditure not specified in the financial schedule (Appendix 5) must be agreed in writing with Sponsor	
13	Relationship between Parties		Neither NHS Trust nor Sponsor can subcontract or pass on any responsibilities without the other Parties’ agreement.	
14	Agreement & Modification		CTA and appendices constitute entire contract. Ensure that anything agreed verbally or by email has been included.	

mCTA section #	Item	Essential items to confirm	Additional issues to consider	Okay? Yes/No
16	Notices	Should be addressed to: The RD&I Manager at the RD&I Department address.		
20	Governing law	Laws of England and Wales	If contract mentions jurisdiction, ensure that English courts have exclusive jurisdiction. Jurisdiction in the courts should be avoided where possible so efforts should be made to include an arbitration process in the CTA.	
Final page	Signatures	NHS Trust Signature: Associate Director of Finance Sponsor signature: Pharmaceutical Company or CRO representative.	Investigator can sign an acknowledgement (only) if desired. To be avoided where possible as has no legal purpose.	
Appendix 1	Protocol	Ensure this is the latest version of the protocol		
Appendix 2	Timelines	Ensure timelines are reasonable	Request updated timelines if start up or signature of CTA is delayed.	
Appendix 3	Clinical trial compensation guidelines	ABPI Guidelines		
Appendix 4	Form of Indemnity	Should follow ABPI guidelines.	May be a separate document. Commercial companies should also provide a copy of the insurance certificate which covers their indemnity cover.	

mCTA section #	Item	Essential items to confirm	Additional issues to consider	Okay? Yes/No
Appendix 5	Financial arrangements	RD&I Finance Co-ordinator should review protocol and ensure all support department costs are covered	Should include set up fee, per patient fee, research governance fee, additional tests, overheads and VAT. Archiving fees if Sponsor does not arrange archiving.	
Appendix 6	PI Conditions	PI may be asked to sign an acknowledgment by sponsor to show agreement to conditions		

6 Amendment History

Version Number:	1.1
Date Of Amendment:	Jan 2019
Details Of Amendment:	Updated Trust and Dept. name; Reduce signature requirement to single senior RD&I Manager.