Sheffield Teaching Hospitals NHS
NHS Foundation Trust

Research Department

STANDARD OPERATING PROCEDURE

Research Department

Execution of Clinical Trial Agreements (CTA) and Clinical Investigation Agreements (CIA) for Commercially Sponsored Clinical Trials

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Approved by	*Research Manager*

Standard Operating Procedure

Execution of Clinical Trial Agreements (CTAs) and Clinical Investigation Agreements (CIAs) for Commercially Sponsored Clinical Trials

This SOP has been produced in accordance with the requirements of The Medicines for Human Use (Clinical Trials) Regulations 2004 and amendments, Research Governance Framework 2005 and ICH GCP Guidelines. This SOP will outline the procedures regarding execution of a contract for commercially sponsored research studies conducted within Sheffield Teaching Hospitals (STH) NHS Foundation Trust.

Background

All commercially sponsored research carried out at Sheffield Teaching Hospitals NHS Foundation Trust 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 and the Association of the British Pharmaceutical Industry 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 appropriate DH/ABPI/ABHI model agreement should be used in all commercially sponsored studies that are conducted within Sheffield NHS Teaching Hospitals Foundation Trust

Definition

A Clinical Trial Agreement or Investigation Agreement is a contract, which describes an agreement between 2 or more persons/institutions that create an obligation to undertake, or refrain from undertaking, a particular action.

The Research Department is responsible for negotiating and executing CTAs and CIAs at Sheffield Teaching Hospitals NHS Foundation Trust; individual investigators may not contractually bind the Trust.

Procedure

The Research Coordinator 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).

1. Review and agreement of the main body and non-financial appendices of the agreement
   1.1. The Research Coordinator confirms that the agreement provided by the company is the appropriate DH/ABPI model agreement in an unmodified format.
   1.2. If the model CTA is not provided or has been modified by the Company, the Research Coordinator contacts the Company to advise the model CTA/CIA is the Trust standard.
   1.3. If the company insists on using a modified or non-model CTA/CIA, the Research Coordinator advises the Company that before consideration by the Research Department the CTA may be reviewed by Trust solicitors at the expense of the Company.
      1.3.1. Using the Commercial Agreements Checklist (Appendix 2) and model CTA/CIA template the Research Coordinator reviews the modified or non-model agreement and confirms whether the content and wording is acceptable.
      1.3.2. The Research Coordinator provides feedback to the Company. If there are any areas of disagreement which the Research Coordinator is unable to resolve, further assistance should be sought from the Trust Solicitor and/or Trust Corporate Governance Department.
   1.4. Where the appropriate DH/ABPI model agreement has been used or where a modified DH/ABPI agreement or non-model agreement have been agreed the Research Coordinator ensures that the:
      - Trust address is correct
      - study and PI details are correct
      - level of compensation is adequate
      - target recruitment number is accurate
      - Trust notices contact information is correct

2. Review of the ICT and agreement of the financial appendix

   2.1. The NIHR Industry Costing Template tariffs are used for all set-up fees, investigations and procedures with local variations applied where local time or cost variations are demonstrable
   2.2. A review of the ICT (sense check and addition of standard local variations) is performed by the Research Department Industry Research Coordinator or delegate(1)
   2.3. A review of the ICT is then performed by applicable support services and study team, and updated per their comments by the Industry Research Coordinator or delegate(1)
   2.4. The R&D Industry Research Coordinator or Research Management Accountant (RMA) reviews the local variations with the sponsor representative via teleconference (2). Study Team and support services representatives will be included as appropriate.
   2.5. The revised local budget is transposed into the Financial Appendix of the model Clinical Trials/Investigation Agreement (mCTA/mCIA) by the sponsor representative
   2.6. A full financial review of the ICT and mCTA/mCIA Financial Appendix is performed by the Research Accountant. Where required, any further changes are negotiated with the sponsor representative by the Research Accountant.

3. Finalisation and signature

   3.1. Once the main body and all appendices of the CTA/CIA have been agreed, the Research Coordinator requests that the sponsor representative finalise the agreement and initiate the signature process.
   3.2. The Research Coordinator arranges signature of the CTA/CIA by the STH R&D Director or other approved signatory.
   3.3. The Research Coordinator returns one copy of the fully executed CTA/CIA to the commercial company, a second copy to the STH PI for the Investigator Site File and a final copy is retained in the R&D Master File.
   3.4. The Research Coordinator saves a scanned copy of the fully executed CTA/CIA to the appropriate section of the Alfresco electronic site file.

4. At authorisation

4.1. The Research Coordinator notifies the Research Accountant, via email, that the study has been authorised.

4.2. On receipt of the authorisation notification the Research Accountant initiates set-up of invoicing and income distribution processes, including financial side letters with other instructions where applicable

(1) For studies hosted by the CRF, the CRF Research Coordinator may coordinate the governance process and undertake this task. For all other studies this task will be undertaken by the R&D Industry Research Coordinator.

(2) For all studies that incur CRF costs, this task will be undertaken by the Research Management Accountant (RMA). For all other studies this task will be undertaken by the R&D Industry Coordinator.

Appendix 1 - Associated Documents

	Document	Research Department Network Location	Website	Database	Created by
1	STH Finance form	Directory\Research Governance\Project Authorisation\Templates	Yes	No	KM
2	Authorisation letter	Directory\Research Governance\Project Authorisation\Templates\authorisation letter	No	No	AL
3	Commercial Agreement check-list	Directory\Research Governance\Project Authorisation\Guidance	No	No	PC
5	Model Agreements	Directory\Research Governance\Project Authorisation\Templates	Yes	No	DoH/ABPI

Appendix 2 - Commercial Agreement STH Research Department Checklist

mCTA section #	Item	Essential items to confirm	Additional issues to consider	Okay? Yes/No
Front page	Agreement	Address should be: STH NHS Foundation Trust Trust Headquarters 8 Beech Hill Road Sheffield S10 2SB		
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 confirnation 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			
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	£2 million cover as minimum. Cover in $ or € of equivalent value is	If the level of cover is below the standard level the Research Coordinator should consider level of risk and cover	

mCTA section #	Item	Essential items to confirm	Additional issues to consider	Okay? Yes/No
		acceptable. An insurance certificate from an insurance company should be made available to cover the amount specified.	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 Research Manager and if in any doubt contact STH Corporate/Legal Governance. 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 Harbor Principles (companies may have statement on data protection/Safe Harbor Principles on their company website). ADD ‘and in line with Confidentiality: NHS Code of Practice Nov 2003’	
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	Avoid a limit on time allowed by Sponsor to find a replacement of PI	Be aware that all expenditure not specified in the financial schedule (Appendix 5) must be agreed in writing with	

mCTA section #	Item	Essential items to confirm	Additional issues to consider	Okay? Yes/No
			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.	
16	Notices	Should be addressed to: Director of R&D at the R&D Department address.		
20	Governing law	Laws of England	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: Director of Research or Medical Director (if conflict of interest or in R&D Director's absence) 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.	
Appendix 5	Financial arrangements	Will be reviewed in detail and signed off by Research Accountant. Research Coordinator should review protocol and ensure all support department costs are	Should include set up fee, per patient fee, research governance fee, additional tests, overheads and VAT. Archiving fees if Sponsor does not arrange archiving.	

mCTA section #	Item	Essential items to confirm	Additional issues to consider	Okay? Yes/No
		covered.		
Appendix 6	PI Conditions	PI may be asked to sign an acknowledgment by sponsor to show agreement to conditions		