Clinical Trials Sponsorship Committee

Background

The Clinical Trials Sponsorship Committee was originally established to consider the University's conduct of clinical trials in scope with the Medicines for Human Use (Clinical Trials) Regulations 2004, when acting either as a sponsor or co-sponsor of such trials. The University has also conducted equivalent international trials outside of the EU regulatory framework. The terms of reference of the Committee is now extended (as of March 2022) to consider review of other clinical trials where similar risk of harm to participants or a statutory risk to the University may present.

Terms of Reference

1. The Committee shall take responsibility for procedure relating to the performance of all interventional clinical trials, either sponsored or co-sponsored (as defined in the UK Policy Framework for Health and Social Care Research, v3.3, November 2017) by the University in accordance with the Policy for Clinical Research[1], where there is a significant risk of physical or psychological harm to participants of the research or a statutory risk to the University. A clinical trial shall mean a study where participants receive a diagnostic, therapeutic, or other type of intervention determined by the study's protocol to evaluate the effectiveness or safety of the intervention in relation to a clinical outcome, or an assessment of non-clinical or purely physiological or other parameter associated with the intervention, and may include, but not limited to, investigation of medicinal products or medical devices, regardless of whether the study is conducted in accordance with a statutory requirement or out of scope of a statutory requirement or an exemption applies. The remit of the Committee includes all clinical trials (highlighted in yellow in section A of Appendix 1) where the focus of the investigation is either a medicinal product (or other substances) or certain categories of medical device or otherwise where the intervention is invasive (delivered through an opening in the skin or other transdermal means of delivery or into a body cavity) or deemed to be burdensome taking into account the nature of the procedures and the vulnerability of the clinical trial subjects (subject to an assessment of risk conducted with the research team). .

2. The Committee shall take responsibility for the development of policies and procedures (including standard operating procedures) to ensure compliance with legal requirements and international standards for the conduct of interventional clinical trials, including, but not limited to:

    - defining the essential requirements in order for the University to sponsor or co-sponsor (with another organisation) clinical trials meeting the criteria set out in (1);
    - defining appropriate standards for the conduct of clinical trials meeting the criteria set out in (1), including procedures to ensure sponsor oversight;
    - monitoring and ensuring compliance of registering clinical trial protocols and reporting of results of all clinical trials (including, but not limited to clinical trials meeting the criteria set out in (1)) in accordance with statutory requirements, a condition of a favourable ethical opinion or applicable codes of practice;

[1] https://www.york.ac.uk/staff/research/governance/research-policies/policy-for-clinical-research/

- recommending revisions to the University's Policy for Clinical Research to the University Research Committee;

3. The Committee shall take overall responsibility for ensuring that the University fulfils its legal duties as a sponsor or co-sponsor, including the decision to sponsor or co-sponsor a clinical trial of an Investigational Medical Product in accordance with the Medicines for Human Use (Clinical Trials) Regulations 2004 or sponsor a Clinical Investigation of a Medical Device conducted in accordance with the Medical Devices Regulations (2002) or the equivalents conducted outside the UK.

4. The Committee shall conduct a formal review of the arrangements for the conduct of clinical trials meeting the criteria set out in (1) prior to the start of the study and shall satisfy itself that the proposed research can be conducted in accordance with all ethical and legal requirements, to appropriate internationally recognised standards[2], and that risks have been appropriately identified, and, where possible, mitigated. The Committee may take in to consideration: (i) a risk assessment conducted by the Contracts and Sponsorship Manager (as the sponsor representative) with the Chief Investigator (in the form included at Appendix 2); (ii) a statement of compliance (in the form included at Appendix 3); (iii) review of clinical trial documentation, including the protocol, information sheet and consent form; and (iv) may request the Chief Investigator to attend a meeting of the Committee. Where a proposed clinical trial is deemed to present particular risks to the University or is proposed to be conducted outside of previously established arrangements, the Committee may request to review the arrangements for the conduct of the study at an early stage, including prior to an application for funding.

5. The Committee shall be notified of clinical trials meeting the criteria set out in (1) submitted for funding and those funded.

6. The Committee shall review reports of clinical trials meeting the criteria set out in (1) in progress, to include, but not limited to, information on recruitment to target, summary safety information and reports of meetings of a trial Data and Safety Monitoring Board. Urgent safety measures shall be communicated to the Committee as urgent business. The completion of clinical trials shall be notified to the Committee.

7. The Committee shall be notified of other clinical trials sponsored by the University not meeting the criteria set out in (1) (as set out in section B of Appendix 1) at the earliest opportunity, either before the start of the clinical trial or at the next available meeting.

8. Clinical or health research outside the scope of these terms of reference is set out in section C of Appendix 1[3].

9. The Committee shall meet at least on three occasions per annum and conduct urgent business electronically, or by arrangement of additional meetings, in the interim.

10. The Committee shall provide the minutes of its meetings to the University Research Committee and the Academic Ethics and Compliance Committee.

[2] ICH E6(R2) Good Clinical Practice https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice

[3] Considerations under the University's Code of practice and principles for good ethical governance (https://www.york.ac.uk/staff/research/governance/research-policies/ethics-code/) and key legal requirements set out in Appendix 1 apply to the conduct of all research involving human participants.

Membership (quorate would be 50% of the membership including the Chair)

Chair
Director of Research, HYMS
Director of York Trials Unit
Director of Research, Innovation and Knowledge Exchange (or delegate)
At least one University clinical academic
One representative from the R&D Unit, York Teaching Hospitals NHS Foundation Trust
At least one other representative from York Trials Unit
Contracts and Sponsorship Manager (sponsor representative), Research, Innovation and Knowledge Exchange
Other University academics (clinical or non-clinical) expert in regulatory requirements applicable to the conduct of clinical trials or research, clinical trial design, management or conduct.

Current membership (February 2022)

Professor Karl Atkin	Chair
Dr Dimitris Lagos	Director of Research, HYMS
Professor David Torgerson	Director of York Trials Unit
Jennifer Gilmartin	Associate Director, Research, Innovation and Knowledge Exchange
Professor Charles Lacey	
Dr Deborah Phillips	York Teaching Hospitals NHS Foundation Trust
Sarah Cockayne	York Trials Unit
Professor Paul Kaye	
Professor Eve Roman	Director, Epidemiology and Cancer Statistics Group
Dr Michael Barber	Contracts and Sponsorship Manager

Appendix 1: Clinical research in scope and out of scope of the Clinical Trials Sponsorship Committee terms of reference and associated legal and other requirements by type of clinical study

	Legal requirements						Protocol registration/legal requirement to post summary results		Insurance & indemnity	
Study type	Data Protection[4]	Section 251 approval[5]	Adults lacking capacity[6]	Human Tissue Act[7]	Clinical Trials Regulations[8]	Medical Devices Regulations[9]	Protocol registration[10],[11]	Posting of results[12],[13]	legal liability	No fault
A. Interventional clinical trials within the scope of oversight of the Clinical Trials Sponsorship Committee										
Clinical trial of an investigational medicinal product (efficacy or safety measures are explicit clinical trial outcomes)	x	X	X	X	x		x	x	x	X

[4] UK General Data Protection Regulation and the Data Protection Act 2018

[5] Section 251 of the National Health Service Act 2006. Applicable where access to patient information without consent. Acts to temporarily lift the common law duty of confidentiality. England and Wales only

[6] Where adults are unable to provide informed consent Mental Capacity Act 2005 (England and Wales) or the Adults with Incapacity (Scotland) Act 2000 applies. Incapacity in trials within scope of the Medicines for Human Use (Clinical Trials) Regulations 2004 are governed by that legislation UK wide.

[7] Human Tissue Act 2004 or Human Tissue (Scotland) Act 2006; Section 45 (Non-consensual testing of DNA) of the Human Tissue Act 2004 applies UK wide. Further information on University procedures for research involving human tissue can be found at: https://www.york.ac.uk/biology/intranet/human-tissue/

[8] Medicines for Human Use (Clinical Trials) Regulations 2004

[9] Medical Devices Regulations 2002

[10] WHO statement on clinical trial registration https://www.who.int/clinical-trials-registry-platform/network/trial-registration

[11] Registration of clinical trials is a formal condition of Research Ethics Committee (REC) favourable opinion https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/#clinical

[12] Legal requirement implemented by Article 57(2) of Regulation (EC) No 726/2004 and Article 41)2) of Regulation (EC) No 1901/2006

[13] WHO Statement on Public Disclosure of Clinical Trial Results https://www.who.int/ictrp/results/WHO_Statement_results_reporting_clinical_trials.pdf

Investigation of medicinal products or other substances where efficacy or safety outcomes are not an objective[14]	x	X	X	X			x	x	x	X
Clinical study of a non-UKCA/CE marked medical device where commercialisation of the product is intended	x	X	X	X		x	x	x	x	X
Clinical study of a non-UKCA/CE marked medical device for use in the institution where commercialisation of the product is not intended	x	X	X	X			x	x	x	X
Clinical study of one or more UKCA/CE marked medical devices for an off-label indication (where the medical device is an invasive medical device[15])	x	X	X	X		Note[16]	x	x	x	
Other clinical trial of a novel intervention or randomised controlled	x	X	X	X			x	x	x	X

[14] Further consideration of what is a medicinal product and whether its use is in scope with the Medicines for Human Use (Clinical Trials) Regulations 2004 can be found at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/949145/Algorithm_Clean__1_.pdf

[15] An invasive device is any medical device introduced into the body, entering either through a break in the skin or an opening in the body. Examples of invasive medical devices include urinary catheters, gastrostomy tubes, stents, implantable devices.

[16] The University should not be deemed the manufacturer of the medical device, else MHRA approval will be required

trial to compare interventions in clinical practice (where the intervention is invasive or deemed burdensome for the participant)										
B. Interventional clinical trials to be notified to the Clinical Trials Sponsorship Committee in accordance with section 7 of the terms of reference										
Clinical study of one or more UKCA/CE marked devices used within the labelled indication	x	X	x	X		Note[17]	x	x	x	
Other clinical trial of a novel intervention or randomised controlled trial to compare interventions in clinical practice (where the intervention is not invasive or deemed burdensome for the participant, subject to a risk assessment)	x	X	x	X			x	x	x	

[17] From 26 May 2021 studies taking place in Northern Ireland require MHRA approval where procedures additional to the normal conditions of use of the device are also invasive or burdensome

C. Clinical or health research outside the scope of the terms of reference of the Clinical Trials Sponsorship Committee										
Scientific investigations involving procedures with human participants that are additional to any clinical care, but do not investigate a novel clinical intervention or involve randomisation between treatment groups[18]	x	X	x	X					x	
Study administrating questionnaires/interviews for quantitative analysis	x	X	x						x	
Study involving qualitative methods only	x	X	x						x	
Study limited to working with human tissue samples	x	X	x	X					x	
Study limited to working with data	x	X	x						x	
Research tissue bank	x	X	x	X					x	
Research database	x	X	x						x	

[18] Examples include imaging investigations (MRI, ultrasound etc), physical examinations, physical tests, computer tests, filming or photography, sample-taking.

Key:

	Clinical Trials under the remit of CTSC

Appendix 2: Risk Assessment Proforma

RISK ASSESSMENT FORM

CHIEF INVESTIGATOR:		**PROJECT TITLE:**	
R&D REFERENCE NUMBER		**SPONSOR:**	University of York
EUDRACT NUMBER:		**CTIMP STUDY:**	YES/NO

STUDY RELATED ACTIVITIES:	MONITORING	YES/NO
	PHARMACOVIGILANCE	YES/NO
	OTHER	

HAZARD CATEGORY **REFER TO R&D/S18**	**HAZARD DESCRIPTION** **ASSIGN EACH HAZARD A SCORE FOR *LIKELIHOOD* AND *IMPACT*** If a particular hazard is: (i) not applicable, state N/A (ii) not listed, enter details under 'other'	**LIKELIHOOD OF HAZARD OCCURING** 1 – Remote 2 – Unlikely 3 – Possible 4 – Likely 5 - Certain	**IMPACT IF HAZARD OCCURS** 1 – Low 2 – Moderate 3 – Significant 4 – Severe 5 – Catastrophic	**RISK** Impact x Likelihood	**Describe what control measures will be put in place to reduce the risk(s) to the lowest possible level.**
RISKS TO PARTICIPANTS' RIGHTS					
Entry into study without fully informed consent					
Failure to act on a participant's request to withdraw from a study					
Failure to protect participants' privacy					
Other – give details					
RISKS TO PARTICIPANTS' SAFETY					
Hazards of the intervention					

HAZARD CATEGORY **REFER TO R&D/S18**	**HAZARD DESCRIPTION** **ASSIGN EACH HAZARD A SCORE FOR *LIKELIHOOD* AND *IMPACT*** If a particular hazard is: (i) not applicable, state N/A (ii) not listed, enter details under 'other'	**LIKELIHOOD OF HAZARD OCCURING** 1 – Remote 2 – Unlikely 3 – Possible 4 – Likely 5 - Certain	**IMPACT IF HAZARD OCCURS** 1 – Low 2 – Moderate 3 – Significant 4 – Severe 5 – Catastrophic	**RISK** Impact x Likelihood	**Describe what control measures will be put in place to reduce the risk(s) to the lowest possible level.**
Hazards of the study assessment methods					
Indemnity arrangements					
Other – give details					
RISKS TO RESEARCHERS					
Lack of experience to carry out responsibilities delegated within study					
Inadequate/outdated or lack of training					
Contact with abusive individuals					
Study proceeding without necessary regulations					
Researcher time					
Other – give details					
RISKS TO COMPLETION OF THE STUDY					
Recruitment and follow-up					
Competency of partner organisations					
Adequacy of study management					
Other – give details					
RISKS TO RELIABILITY OF RESULTS					
Lack of study power					

HAZARD CATEGORY **REFER TO R&D/S18**	**HAZARD DESCRIPTION** **ASSIGN EACH HAZARD A SCORE FOR *LIKELIHOOD* AND *IMPACT*** If a particular hazard is: (i) not applicable, state N/A (ii) not listed, enter details under 'other'	**LIKELIHOOD OF HAZARD OCCURING** 1 – Remote 2 – Unlikely 3 – Possible 4 – Likely 5 - Certain	**IMPACT IF HAZARD OCCURS** 1 – Low 2 – Moderate 3 – Significant 4 – Severe 5 – Catastrophic	**RISK** Impact x Likelihood	**Describe what control measures will be put in place to reduce the risk(s) to the lowest possible level.**
Setting the wrong eligibility criteria					
Major violation of Eligibility criteria					
Fraud					
Randomisation procedure					
Outcome assessment					
Data being incomplete and inaccurate					
Non-adherence to the protocol, GCP or SOPs					
Other – give details					
RISKS TO ORGANISATION					
Research project inaccurately costed					
Routine clinical services affected					
Other – give details					

DECLARATION OF Chief Investigator (CI)			
As the CI of the above study, I declare that the above Risk Assessment is true and complete to the best of my knowledge			
Name:		Signature:	
CI:		Date (dd/mm/yyyy):	

Sponsor Representative		Date (dd/mm/yyyy):		Signature:

RISK ASSESSMENT MATRIX

IMPACT	LIKELIHOOD				
	1 Remote	**2 Unlikely**	**3 Possible**	**4 Likely**	**5 Certain**
1 Low	1	2	3	4	5
2 Moderate	2	4	6	8	10
3 Significant	3	6	9	12	15
4 Severe	4	8	12	16	20
5 Catastrophic	5	10	15	20	25

RISK MANAGEMENT KEY

Action and time scales
Immediate action must be taken to manage the risk. Control measures should be put in place which will have the effect of reducing the impact of an event or the likelihood of an event occurring. A number of control measures may be required.
Significant resources may have to be allocated to reduce the risk. Where the risk involves work in progress urgent action should be taken.
Effort should be made to reduce the risk, but the costs of prevention should be carefully measured and weighed against the impact of the event. Establish more precisely the likelihood of harm as a basis for determining the need for improved control measures.
On or below this level a risk is acceptable. Existing controls should be monitored and adjusted. No further action or additional costs are required. Consideration may be given to a more cost-effective solution or improvement that imposes no additional cost burden.
Acceptable risk. No further action or additional controls are required. Risks at this level should be monitored, and reassessed at appropriate intervals.

Appendix 3: Statement of Compliance/Sponsor Checklist Proforma

STATEMENT OF COMPLIANCE/SPONSOR CHECKLIST

UoY Reference	**Study Title**	Chief Investigator

Assessment criteria	**Comments**	**Check Complete**	Date
Review of protocol	• Reference safety information & adverse event reporting • Unblinding • Indemnity arrangements • Procedures for notifying the end of trial • Protocol registration		
Review of information sheet and consent forms	• Are research procedures adequately described and aligned with the protocol • Right to withdraw • Data processing/legal basis • Indemnity arrangements • Consent for genetic analysis		
Indemnity arrangements	• Legal liability or no fault		
Peer review			
Experience of Chief Investigator/research team			
Procurement, transport, storage and administration of medicinal products			
Material transfer provisions and sample analysis			
Compliance with prevailing data protection legislation/data security			
Other legal requirements			
Arrangements for data and statistical analysis			
Assessment of contractual arrangements	• Appropriate delegation of trial activities • Compliance with prevailing legal requirements		
Trial governance arrangements	• Has a Data and Safety Monitoring Board been established?		
Monitoring plan/arrangements			
Arrangements for registration of trial protocol			

Legal requirement to post summary trial results			
Risk assessment conducted with Chief Investigator			
Review of trial specific standard operating procedures			
Additional comments			
Relevant University of York Ethics Committee approval obtained			
Relevant favourable opinion obtained in jurisdiction where trial conducted			
Relevant clinical trial authorisation obtained in jurisdiction where trial conducted			
Other regulatory approvals and authorisations received			

Signature of sponsor representative	**Status**	**Date**	
	Interim		
	Final		