RESEARCH & ENTERPRISE SERVICES
RESEARCH ETHICS, INTEGRITY & GOVERNANCE

UNIVERSITY OF SUSSEX

Standard Operating Procedures for Sponsorship Approval of CTIMPs

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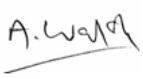
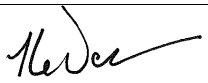
Author: Antony Walsh **Designation:** RES Research Governance Officer	*Signature* 	*Date* 25 August 2020
Authorised by: Kevin Davies **Designation:** SSC Chair		

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1.0	1 September 2020	-

Disclaimer

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[1] http://www.sussex.ac.uk/staff/research/governance

1 Purpose

1.1 This SOP describes the processes that are involved for obtaining University of Sussex (US) sponsorship approval, for research projects led by staff from US and where funding bodies require a Sponsor to be identified as part of the application; and which fall under the UK Policy Framework for Health and Social Care Research (2017), and the Medicines for Human Use (Clinical Trials) Regulations 2004.

1.2 The scope of the document is for all schools at the University of Sussex, all members of staff with substantive employment and students registered at the University (including Brighton and Sussex Medical School).

1.3 The EU Good Clinical Practice (GCP) Directive 2001/20/EC was introduced to establish standardisation of research activity in Clinical Trials throughout the European Union. It was transposed into UK law as the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) which came into force on 1 May 2004. The Medicines for Human Use (Clinical Trials) Regulations together with subsequent amendments will be referred to as the Regulations in the rest of this document[2].

1.4 Regulation 3, as amended by Statutory Instrument 2006/1928, requires that a Clinical Trial of an Investigational Medicinal Product (CTIMP) has to have a named Sponsor. As stated in the Regulations, the role of the Sponsor "in relation to a clinical trial, [is] the person who takes responsibility for the initiation, management and financing (or arranging the financing) of that trial"[3]. Therefore, all proposed research which falls within the scope of the Regulations will require a formal confirmation from the Sponsor.

[2] http://www.legislation.gov.uk/uksi/2004/1031/pdfs/uksi_20041031_en.pdf
To find out if the study is a CTIMP applicants should use the MHRA's algorithm ***Is it a clinical trial of a medicinal product?***
[3] http://www.legislation.gov.uk/uksi/2006/1928/pdfs/uksi_20061928_en.pdf

2. Introduction

2.1 The University of Sussex, through its *Code of Practice for Research* is committed to promoting and upholding the highest quality academic, professional and ethical standards in all its activities and seeks to foster a culture of professional integrity.

Good Clinical Practice (GCP)

2.2 The University expects that *all clinical research involving human participants* is undertaken in line with the principles of GCP.

2.3 Good Clinical Practice (GCP) is an international ethical and scientific quality standard for the design and conduct of clinical research involving humans. GCP is a set of core principles, which applies to all clinical investigations that could affect the safety and wellbeing of human participants. GCP is internationally recognised as best practice and compliance (including up to date training) and is a legal obligation in the UK/Europe for all trials of investigational medicinal products. GCP was developed by the regulatory authorities represented in the Tripartite International Conference on Harmonisation and provides international assurance that:

(i) Data and reported results of clinical investigations are credible and accurate, and;
(ii) The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.

3. Responsibilities

Chief Investigator

3.1 The *Chief Investigator* (CI) is responsible for making a request to the University of Sussex to act as Sponsor and fulfilling the terms of the 'Conditions of Sponsorship Agreement' issued when the study has been formally accepted for Sponsorship. The CI may delegate the activities described in this SOP to sufficiently experienced members of the research team or Professional Support Services (e.g. the Joint Clinical Research Office (JCRO)) or a Clinical Trials Unit, however the final responsibility for ensuring compliance with the SOP's requirements will remain with the CI.

The Sponsor

3.2 The UK Policy Framework for Health and Social Care Research (2017) stipulates that 'The *Sponsor* has overall responsibility for the research, including:

a. identifying and addressing poorly designed or planned research and poor-quality research proposals, protocols or applications and ensuring that research proposals and protocols:
   - take into account systematic reviews of relevant existing research evidence and other relevant research in progress,
   - make appropriate use of patient, service user and public involvement and
   - are scientifically sound (e.g. through independent expert review), safe, ethical, legal and feasible and remain so for the duration of the research, taking account of developments while the research is ongoing;

b. satisfying itself that the investigators, research team and research sites are suitable;
c. ensuring that roles and responsibilities of the parties involved in the research and any delegation by the sponsor of its tasks are agreed and documented;
d. ensuring adequate provision is made for insurance or indemnity to cover liabilities which may arise in relation to the design, management and conduct of the research project; and
e. ensuring appropriate arrangements are made for making information about the research publicly available before it starts (unless a deferral is agreed by or on behalf of the research ethics committee); agreeing appropriate arrangements for making data and tissue accessible, with adequate consent and privacy safeguards, in a timely manner after it has finished; and ensuring arrangements for information about the findings of the research to be made available, including, where appropriate, to participants;
f. ensuring that, where expected or required, the research has approval from a research ethics committee and any other relevant approval bodies before it begins;
g. verifying that regulatory and practical arrangements are in place, before permitting the research to begin in a safe and timely manner;
h. putting and keeping in place arrangements for adequate finance and management of the research project, including its competent risk management and data management;
i. ensuring that effective procedures and arrangements are kept in place and adhered to for reporting (e.g. progress reports, safety reports) and for monitoring the research, including its conduct and the ongoing suitability of the approved proposal or protocol in light of adverse events or other developments.'[4]

3.3 *Formal confirmation from the designated Sponsor **must** be obtained prior to an application for Host Organisation or NHS Research Ethics Committee (REC) approval.*

3.4 In an instance where the University is asked to assume full and sole responsibility for a CTIMP the University will usually expect it to be managed within a Clinical Trials Unit (CTU) or an organisation with equivalent proven experience in providing oversight and management to such studies. The University will undertake due diligence to confirm this experience.

4. Procedure

4.1 The Chief Investigator (CI) is required to submit a formal application for Sponsorship without which no external approvals for research will be granted.

How to determine whether the University of Sussex is the likely Sponsor

4.2 The University of Sussex will review Sponsorship requests for research projects where:

- The substantive employer of the CI is the University of Sussex
- The NHS partner will not act as Sponsor;
- The third-party partner will not act as Sponsor;
- The research project does not have an NHS or third-party partner

[4] UK Policy Framework, pp. 23-24

- The project is related to an academic qualification and the University is likely to be able to provide sponsorship on the basis of being able to provide acceptable oversight and the management of appropriate levels of risk given the institution's status as an educational establishment

Who should request Sponsorship ?

4.3 It is the responsibility of the CI on a project to request Sponsorship. However, it is recognised that this responsibility may be delegated to another member of the research team with sufficient knowledge of the research activity.

How and When to request Sponsorship?

Prior to submission of an application for funding – Application for' Sponsorship in Principle' for a CTIMP

4.4 The CI should liaise with University Research Governance Officer as early as possible in the study planning process to discuss potential sponsorship ('sponsorship in principle'). The CI is expected to formally request Sponsorship once funding for a research project has been confirmed.

4.5 In circumstances where the funding body requires confirmation of Sponsorship prior to submission of the funding application, the CI should contact the Research Governance Officer in Research and Enterprise Services (researchsponsorship@sussex.ac.uk).

4.6 The following should be submitted for the purposes of: 'sponsorship in principle'

a) Confirmation of who the CI is and a copy of their CV (updated within the last 2 years)
b) Confirmation of the clinical trial phase for the trial
c) Confirmation that the proposed study is classed as a CTIMP if applicable
d) An outline trial protocol to enable the sponsor to risk assess the trial and categorise the potential risk associated with the IMP (Investigational medicinal product), (Type A, B or C) http://www.ct-toolkit.ac.uk/routemap/riskassessment/
e) Confirmation of engagement with a statistician and statistical review
f) Confirmation of a data management plan
g) Confirmation of peer-review and Head of School approval
h) Details of costings carried out to date: costings must include costs for a clinical trials unit involvement, costs for MHRA fee, archiving costs, costs for the IMP and placebo, pharmacy costs and any other research costs
i) An outline of proposed trial timelines from idea to archiving, including all submission deadlines
j) Confirmation that the lead NHS R&D site has agreed to host the CTIMP(s) in principle and confirmation of the involvement of other host organisations
k) The name of the proposed lead pharmacist and evidence of in principle acceptance by the pharmacist and the pharmacist's employer

l) Confirmation of vendors likely to be used in the trial and confirmation (at least in principle) of what activity they will be providing (e.g. CTU, IMP distributor, randomisation service, GMP facility,
m) Laboratories) – each vendor to be listed separately
n) Proposed archiving arrangements and costs

4.8 The University will require the following information about the proposed CTU who will be supporting the Trial:

a) A complete list of activities the CTU has agreed to provide for the trial (please point out any cost related activities the CTU has not agreed to carry out)
b) Confirmation regarding the level of trial management that the CTU will provide and what the
c) CTU expects the Sponsor/CI to undertake
d) Confirmation of the IMP costs, including any manufacturing, labelling, distribution and storage costs the CTU has provided for this trial
e) Confirmation of who the lead pharmacist for this trial is, as agreed with the CTU, including their role and responsibility
f) Confirmation of the proposed level of monitoring for this trial as agreed with the CTU
g) Any issues the CTU has raised for this application that remain unresolved
h) Any issue where in the opinion of the CTU there is a lack of clarity e.g. is there an activity that hasn't been considered or costed or is there uncertainty about who is or should be providing the activity

Applying for University Sponsorship following award of funding – the Sponsorship Sub-Committee

4.9 The University has a Sponsorship Sub-Committee that has overarching oversight of all Sponsorship approvals and subsequent activities. The details of its meetings (including dates of submission deadlines) are to be found at:
http://www.sussex.ac.uk/staff/research/governance/sponsorship/applysponsorship

4.10 Once funding has been secured, applicants should consult the Checklist for University Sponsorship (see Appendix B below) before starting their formal Sponsorship application to ensure the appropriate documentation is ready for submission for Sponsorship review.

4.11 In addition to the documents identified in 4.7 above, the following documents should be enclosed, numbered, dated and sent to: researchsponsorship@sussex.ac.uk :

- Covering letter to the Head of the Chair of the Sponsorship Sub-Committee (max 1 side of A4).
- Completed draft IRAS (Integrated Research Application System) Form (www.myresearchproject.org.uk).
- Research protocol
- Participant Information Sheet for each group of participants involved in the study with a new version number and date in the footer of the document

- Consent form for each group of participants involved in the study with a new version number and date in the footer of the document
- Recruitment materials: emails / posters / letter of approach to for e.g. GPs; gatekeepers; interview schedules and topic guides
- Any validated questionnaires to be used
- Researcher designed questionnaires
- Summary CVs for all investigators and Good Clinical Practice (GCP) certificates of the research team.
- Study Risk Assessment/Management Plan
- Risk Categorisation Template
- If prior study review has occurred within NHS R&D, an overview of the outcomes of this process
- If the study is in Primary Care, please state whether the Clinical Research Network (CRN) has been engaged in relation to providing support
- Organisational Information Document
- HRA Schedule of Events Cost Attribution Template (SoECAT)
- Confirmation of Funding letter and evidence of management authorisation of the study

The HRA may change the requirements for documents submitted for HRA and NHS REC review and approval. CI's should check the latest available information on the HRA website[5]

4.12 The Committee cannot review and decide on applications that are missing required minimum documentation.

4.13 The Sponsor will perform a further risk assessment. The study team will also be asked to complete a Study Risk Assessment/Management Plan and a Risk Categorisation Template.

4.14 Before agreeing to take on the role of Sponsor, US must satisfy itself that appropriate systems, capacity and expertise are in place and any risks are mitigated or deemed as acceptable to the University. Risks which could be posed by the study include lack of available resource or lack of experience / capacity within US itself to act as Sponsor for the given Study.

After the Meeting

4.15 There are three main decision outcomes from the meeting:

a) Full approval of the application as submitted. A letter will be issued by the Sponsor's Representative confirming the University's Sponsorship.

[5] https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/hra-approval/

b) Provisional approval pending the addressing of issues identified[6]. If minor, Chair approval can be granted outside of the Committee cycle.

c) Rejected with comments. If the changes required to approve sponsorship are deemed to require re-application. The University reserves the right to refuse sponsorship if the research study cannot be adequately supported or it does not meet relevant regulatory requirements.

4.16 Further information and/or documentation may be requested of the CI as necessary.

4.17 Wherever possible, the Sub-Committee will request the resubmission of amended applications in response to review between meetings to avoid delays to the commencement of research. In exceptional circumstances the Chair may request that a resubmission be only considered at the next meeting of the Sub-Committee.

4.18 The Sponsorship Sub-Committee may delegate the responsibility for review of new applications for Sponsorship but cannot divest itself of its sponsor responsibilities.

Right to withdrawal of Sponsorship

4.18 In line with its responsibilities as a recognised Sponsor of research, the University (through the Sponsorship Sub-Committee) may withdraw Sponsorship that it has granted if there has been a breach of the 'Conditions of Sponsorship Agreement' or if matters come to light through the study that have significant legal, regulatory, financial or reputational consequences to the University.

5. Training

5.1 This is a 'read and understand' SOP. Please note that the Research Governance Office discourages the retention of hard copies of SOPs and can only guarantee that the most up-to date version is on the University website.

6. Abbreviations

CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational or Medicinal Product
CTU	Clinical Trials Unit
CV	Curriculum Vitae
EU	European Union
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice

[6] The Sub-Committee, upon decision of the Chair, may delegate the checking of issues identified to the Secretary, a selection of members or request that the application be reconsidered by the whole Sub Committee.

GP	General Practitioner
HRA	Health Research Authority
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IMP	Investigational or Medicinal Product
ISF	Investigative Site File
IRAS	Integrated Research Application System
JCRO	Joint Clinical Research Office
MHRA	Medicine and Healthcare Products Regulatory Agency
NHS	National Health Service
PI	Principal Investigator
PIS	Patient Information Sheet
R&D	Research and Development
REC	Research Ethics Committee
REIGO	Research Ethics and Integrity Office
SOECAT	Schedule of Events Cost Attribution Template
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reactions)
TMF	Trial Master File
US	University of Sussex

7.Cross Referenced SOPs

SOPRG04	Risk Assessment
SOPRG03	Notification of Serious Breaches of Good Clinical Practice or the Trial protocol
SOPRG05a	Monitoring CTIMP research Studies
SOPRG09a	Procedures for Close out of a CTIMP
SOPRG010	Delegation of roles and responsibilities
SOPRG16	Amendments, Urgent Safety Measures and Temporary Halt to a Trial
SOPRG17a	CTIMP Data Management
SOPRG21	Adverse Events in CTIMPs
SOPRG33	Archiving Paper Trial Documents (for University of Sussex as a Sponsor)
SOPRG35	Trial Reporting, Project Publication and Dissemination

8. References

Clinical Trials Regulations 2004 (SI 2004/1031)
http://www.legislation.gov.uk/uksi/2004/1031/pdfs/uksi_20041031_en.pdf

Clinical Trials Regulations 2006 (SI 2006/1928)

http://www.legislation.gov.uk/uksi/2006/1928/pdfs/uksi_20061928_en.pdf *UK*

Policy Framework Health and Social Care Research

https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/ukpolicy-framework-health-social-care-research/

Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments
http://www.legislation.gov.uk/uksi/2004/1031/contents/made

Is my study research?, Medical Research Council – http://www.hradecisiontools.org.uk/research/

Is it a Clinical Trial of a Medicinal Product?, Medicines and Healthcare Regulatory Agency (MHRA)
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/317952/Algothrim.pdf

NIHR Clinical Trials Toolkit - http://www.ct-toolkit.ac.uk/

Code of Practice for Research, University of Sussex
http://www.sussex.ac.uk/staff/research/documents/code.pdf

Good Clinical Practice, International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use

https://www.ich.org/page/efficacy-guidelines

APPENDIX A: Conditions of Sponsorship Agreement

Conditions of Sponsorship Agreement

The University of Sussex will act as Sponsor, as defined by the Medicines for Human Use (Clinical Trial) Regulations 2004 and the UK Policy Framework for Health and Social Care Research (2017) for the above research project provided that the Chief Investigator adheres to the following conditions of sponsorship:

a) HRA approval has been received for the study.

b) Confirmation of Capacity & Capability is received from relevant NHS Trusts before any patients or participants are recruited.

c) The CI (Chief Investigator) and members of the **research** team will comply with all applicable regulations; including the principles from the UK Policy Framework for Health and Social Care Research (2017) the Medicines for Human Use (Clinical Trials) regulations 2004 and subsequent amendments (if a CTIMP), ICH GCP, the Data Protection Act 1998, the Human Tissue Act 2004 and any other relevant guidance and/or legislation.

d) The CI and members of the research team will comply with the University's *Code of Practice for Research*[1]

e) All research team members are appropriately GCP trained throughout the duration of the study.

f) Ensuring that the study is registered on an appropriate registry prior to recruitment of the first patient if applicable.

g) Ensuring that the clinical trial data is generated, documented and reported in accordance with the protocol, GCP and regulatory requirements.

h) A delegation log is completed and kept up to date throughout the duration of the trial.

i) A Trial Master File (TMF) must be set up containing essential documents in accordance with the Trial Master File Index provided and must be maintained throughout the research study.

j) If deemed appropriate by the Sponsor, a site initiation meeting is performed before the study commences and research staff training in the protocol is documented.

k) The research study is conducted in accordance with the protocol and any significant deviations are reported to the Sponsor (researchsponsorship@sussex.ac.uk).

) Any proposed amendments to the research study are submitted to researchsponsorship@sussex.ac.uk for review and approval as per the Standard Operating Procedures for Sponsorship Approval.

m)Serious Adverse Events (SAEs) are reported to the Sponsor immediately and according to the study's protocol.

n) All SAEs are assessed in order to determine whether the SAE is a Suspected Unexpected Serious Adverse Reaction (SUSAR) as well as any new safety information that becomes available during the trial. SUSARs should be reported to the MHRA within the required time-frame.

o) If the study is a CTIMP, Development Safety Update Reports are submitted annually to the Sponsor prior to review by the relevant authorities.

p) Annual Progress Reports are submitted to the Sponsor and the REC.

q) Urgent Safety Measures (USM) must be notified to the Sponsor, MHRA and the REC within 3 days of implementing the measure.

r) Any serious breaches of GCP or the protocol must be reported to the Sponsor, MHRA and the REC immediately.

s) Any other correspondence between the MHRA and the REC is copied to the Sponsor (researchsponsorship@sussex.ac.uk).

t) The Trial Master File (TMF) and other associated documentation must be made available for monitoring, auditing or inspection purposes.

u) At the end of the study, an End of Trial Notification/Declaration is sent to the Sponsor, the MHRA (if applicable) and the REC within 90 days of the end of the study, or within 15 days if the trial is terminated prematurely.

v) The end of trial study report must be submitted to the Sponsor, the MHRA (if applicable) and the REC within one year of the end of the trial.

w) The study documentation must be archived in accordance with the applicable University policies.

x) The Chief Investigator will ensure appropriate oversight of the study at all times and agrees to meet with the Sponsor for a Sponsor Review Meeting at intervals agreed at the time of sponsorship.

By signing the declaration on IRAS form, I agree to adhere to the above conditions of sponsorship.

Please notify researchsponsorship@sussex.ac.uk when the first participant has been recruited

APPENDIX B: University Sponsorship Application Document checklist

**** Please ensure that you download the latest copy from**
http://www.sussex.ac.uk/staff/research/governance/sponsorship/applysponsorship

Document (answer if applicable)	Version	Dated	Doc no.	Included Yes/No
Letter to Chair of the Sponsorship Sub-Committee (brief overview and justification – max 1 side A4)				
Completed draft IRAS [1] form				
Research Protocol [2] or sufficient detail provided in documentation				
HRA Schedule of Events Cost Attribution Template (SoECAT) [3]				
UK Local Information Pack [4] (comprising of the Organisation Information Document [5] (OID), HRA Delegation Log [6], draft text of covering email using standard template format [7][6])*				
Summary CV for Chief/Principal Investigator and/or GCP certificates of research team (if applicable e.g. for Clinical Trials or medical device studies)				
Participant Information Sheet [8]				
Invitation Letter or email text copy to participant/s and volunteers				
Letter to Gatekeeper				
Participant Consent form [9]				
Interview schedules, topic guide, interview questions or questionnaire				
Validated questionnaire(s) and non-validated questionnaire(s)				
Recruitment materials for research participants				
Evidence of financial support (funding letters etc.) and evidence of management authorisation of the project				
#Overseas Travel Safety and Security Risk Assessment form [10]				
Evidence of sufficient funding arrangements and resource				
#For student projects: Evidence of adequate (if overseas, local field) supervision in place				
#For projects intended for NIHR Portfolio adoption – Portfolio application form and proof of **two** independent peer reviews [11]				
If prior study review has occurred within NHS R&D, evidence of the outcomes of this process				
If the study is in Primary Care, please state whether the CRN has been engaged in relation to providing support [12]				

- Documents should be sequentially numbered within their file name and version control identified in their footer.
- Prior to submission you are advised to check the dates of forthcoming Sponsorship Sub-Committee meetings (http://www.sussex.ac.uk/staff/research/governance/sponsorship/applysponsorship)
- **All queries and submissions to researchsponsorship@sussex.ac.uk**

[13] http://www.sussex.ac.uk/hso/specialist/riskass/fieldworkriskassessment/otssra

[14] https://www.nihr.ac.uk/research-and-impact/nihr-clinical-research-network-portfolio/

[15] https://www.nihr.ac.uk/about-us/how-we-are-managed/managing-centres/crn/