Sponsorship and Insurance Approval

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Version	Date	Reason for Change
Version 1.0	14 Sep 2006	Annual review
Version 2.0	25 Jun 2007	Annual review, change in practice post MHRA inspection
Version 3.0	02 Jul 2008	Annual review
Version 4.0	08 Feb 2010	Formation of Joint Research Office
Version 5.0	14 Jul 2011	Annual Review
Version 6.0	30 Nov 2012	Annual Review
Version 7.0	18 Feb 2015	Scheduled Review and addition of communication with Sponsor's Representatives
Version 8.0	25 Oct 2017	Scheduled Review, Addition of Legal Representative Risk assessment tool, factors posing risk on sponsorship. CI Agreement for CTIMP and Guide on sponsorship has been updated Minor/administrative changes
Version 9.0	18 Feb 2019	Sponsorship and Insurance registration form appendix addition
Version 10.0	19 Oct 2020	Scheduled Review Templates removed and administrative changes to SOP. JRCO name change to RGIT.

Version 11.0	21 Oct 2020	Amended section 4.4.2.1 for further clarifications
Version 12.0	05 Jul 2021	Minor change made to the to the Appendices/Templates section
Version 13.0	02 Nov 2021	Inclusion of CWOW IRAS form

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1. PURPOSE

This SOP describes the process for obtaining sponsorship approval and registering a project for insurance cover. It applies to all studies falling under the UK Policy Framework for Health and Social Care Research and the Medicines for Human Use (Clinical Trials) Regulations 2004.

The SOP also outlines the process for Clinical Trials of Investigational Medicinal Products (CTIMP) studies where Imperial College London or Imperial College NHS Trust agree to act as EU Legal Representative on behalf of a sponsor based outside of the European Economic Area (EEA).

A UK legal representative of the lead sponsor (or any co-sponsor) is not required for non-CTIMP studies.

2. INTRODUCTION

Every clinical trial/research study must have a named sponsor. A sponsor is defined in Article 2(e) of Directive 2001/20/EC as "an individual, company, institution or organisation which takes responsibility of the initiation, management and/or financing of a clinical trial".

The UK Policy Framework for Health and Social Care states that for non-commercial research the sponsor is normally expected to be the employer of the chief investigator. For commercial research the funder is usually the sponsor. It defines the sponsor as having responsibility for ensuring effective arrangements are in place to set up, run and report a research project.

All Imperial College Academic Health Sciences Centre (AHSC) healthcare research projects which involve humans, their tissue and/or data must be registered and assessed for sponsorship with the Research Governance and Integrity Team (RGIT). This applies to studies funded by Imperial College AHSC or another organisation (including a commercial company); whether it is a clinical trial of an IMP or device; human tissue or data project; observational or epidemiological study; or physiological study. Although please note, for Imperial College AHSC studies where the only research being undertaken at Imperial is tissue collection (e.g. collecting biopsies, blood only), registration and ethics approval may be obtained from the Tissue Bank, who have been delegated authority from the REC to approve this type of project. Contact the Imperial Tissue Bank for advice.

Registration allows the RGIT to:

- Assess the project for AHSC sponsorship
- Confirm or arrange appropriate insurance cover for the study
- Discuss research governance issues, if required
- Have sponsor oversight
- Ensure the study has the necessary regulatory approvals

- Have an overview of the AHSC's clinical research portfolio
- Respond to monitoring/audit requests by regulatory authorities

Appendix 1 contains a guide to help determine who should act as study Sponsor.

3. RESPONSIBILITIES

This SOP must be followed by the RGIT and the Chief Investigators (CI) and clinical trial teams of all proposed Imperial College AHSC sponsored studies. RGIT staff members must comply with this SOP when assessing, reviewing and providing sponsorship for a project.

Any study coming in to RGIT for sponsorship we check with research integrity team tracker if up to date with final reporting requirements on public database – must be confirmed before the sponsor review starts

The Head of Research Governance and Integrity is responsible for ensuring that this SOP is updated by the review date, or as necessary.

4. PROCEDURE

4.1. WHEN TO REGISTER WITH THE RGIT

All research projects sponsored by Imperial College AHSC must be registered with the RGIT. Registration must occur **prior** to the submission of the application for approval to REC/HRA/MHRA (as applicable to the study). The approvals required will vary according to type of study being submitted. The RGIT will assess on which approvals are needed.

For projects occurring within Imperial College Healthcare NHS Trust, registration will form part of the Confirmation of Capacity and Capability (CCC) process, which must be in place before the study starts (see RGIT_SOP_031).

4.2. FOR PROJECTS TO BE SPONSORED BY IMPERIAL COLLEGE AHSC:

4.2.1 To register a project with the RGIT:

Send the following to RGIT@imperial.ac.uk:

- A completed RGIT Sponsorship and Insurance Request Form .
- CV for Chief/Principal Investigator
- Protocol, Participant Information Sheet and Informed Consent Form in word format and following RGIT SOP templates. Word versions can be requested from RGIT.
- Ethics application form (full IRAS dataset or ICREC/SETREC) For CTIMP studies the Combined Ways of Working (CWOW) IRAS form should be completed and the RGIT notified when it is ready to review in the system
- Non-commercial Organisational Information Document (OID) or model non-commercial agreement (mNCA). See Appendix 5 for guidance on which one to use.
- Schedule of Events or Schedule of Events Cost Attribution.
- Funding letter or funding agreement, if applicable

Additional documentation required for CTIMP studies:

- CTIMP addendum and provide confirmation that the College's approved Electronic Data Capture system for CTIMPs will be used See RGIT_SOP_030 for details.
- Cover letters for the MHRA and REC submissions outlining title, phase of study, whether the study is a Type A classification, confirmation of where the RSI (Reference Safety Information) can be found and documents you intend to submit (including versions/dates)
- All IMP related documentation – IB/IMPD/SMPC as required
- Manufacturer's authorisation, including the importer's authorisation and Qualified Person declaration on Good Manufacturing Practice for each manufacturing site if the product is manufactured outside the EU (this should be provided to you by the manufacturer)
- Labelling documentation: In line with RGIT SOP IMP Management
- Confirmation that trial monitoring will be in place for non-ICHT sites where relevant
- Any previous correspondence with the MHRA regarding the study

4.2.2 What happens next?

If the study is a CTIMP it will go to the CTIMP team for review. Non-CTIMPS will be allocated for review to the next available person at RGIT (Clinical Trials Manager (CTM), Research Governance Manager (RGM) or Clinical/Research Facilitator (RGF).

The CTM/RGM/RGF allocated the study will check if it has already been registered by ICHT on DOCUMAS® (AHSCs electronic database) during a grant application process and if not they will register the study on the database.

Prior to any sponsor review activities occurring, the CTM/RGM/RGF allocated the study will check with the Research Integrity Officer at RGIT to ensure that the CI has completed all final reporting requirements for public databases (e.g. CTgov, EudraCT). The CI will be notified of any gaps in reporting by the CTM/RGM/RGF, who will also copy in the Research Integrity Officer, who will be able to advise the study team on resolving reporting issues. All final reporting requirements must be resolved by the study team and confirmation of resolution confirmed to the CTM/RGM/RGF by the Research Integrity Officer before the sponsor review can proceed. The only exception to this will be for Master's students' studies, which have short timelines and should not be held up due to any CI failure to meet public database reporting requirements.

Following registration, if the study is running at ICHT, the CTM/RGM/RGF reviewing for sponsorship will send the completed RGIT form with the DOCUMAS reference number to the relevant Divisional Research Manager (DRM) to facilitate feasibility checks and set up at ICHT. A list of the DRMs can be found in RGIT_SOP_031.

If the study is sponsored by Imperial College, is running at ICHT as a single site and uses an OID, then the OID should be sent to the ICHT JRO contracts team for review at imperial.admin_trustresearchcontracts@nhs.net See RGIT_TEMP_022 for further details.

If the study is unfunded and due to run at ICHT, the CTM/RGM/RGF will check with the DRM, prior to commencing the sponsor review, that the Trust will be able to support the research. This confirmation must be received in writing before the sponsor review can start. Unfunded research due to run at Imperial College London should have authorisation from the relevant College Head of Department.

Immediately following DOCUMAS registration, the CTM/RGM/RGF will also check if the study needs to be assessed by the RGIT Peer Review Office, in accordance with the procedure set out in RGIT_SOP_040

The CTM/RGM/RGF will aim to provide the initial sponsor review, following receipt of all relevant documents listed in 4.2.1, within 5 working days. They will advise on research governance issues, if needed and can meet with the study team to discuss the study.

4.2.2.1 Assess for Imperial College AHSC Sponsorship, where applicable

In order for Imperial College London or Imperial College NHS Trust to act as the research Sponsor, the CTM/RGM/RGF will assess the project for risk to College or Trust and participants, using risk assessment tool templates. A decision on sponsorship will then be made, in consultation with the Head of Research Governance and Integrity if needed.

Factors that are likely to pose a risk in the conduct of a trial include, but are not limited to:

- Insufficient funding
- CI's lack of experience
- Certain groups of patients e.g. pregnant women, children, vulnerable adults
- Trials that are excluded or restricted in terms of insurance
- Trial complexity in terms of design, size and involvement of multi-centre and/or multinational trials
- Involvement of Advanced medicine therapy product
- For CTIMP trial - Involving a medicinal product not licensed in any EU Member State

4.2.2.2 Assess and confirm insurance cover

Appropriate insurance must be in place for each research project undertaken in order to cover against harm to a research participant. There are two types of possible harm: negligent and non-negligent.

Negligent Harm: Any action or process that is held by a court to have caused harm because of a lack of due diligence, lack of care, omission of duty or an act of carelessness towards a participant in a research project.

Non-Negligent Harm: Circumstances where there is no specifically identified causative factor relating to the harm of a participant in a research project, but harm is likely, on the balance of probabilities, to have arisen from the participant taking part in the research.

Not all projects will need cover against both types of harm. The RGIT are responsible for determining what insurance is relevant to a research project.

The insurance assessment should provide the CI with the reassurance that the study has the appropriate level of protection.

Due to certain exclusions in Imperial College policies, the study team must not assume that insurance will apply to a project until it has been confirmed to the CI in writing. Where necessary, the RGIT may need to refer to the College's Insurance and Indemnity Manager or Insurers for further assessment.

As it can be complicated to arrange insurance for overseas research, the study team should contact RGIT as early as possible to discuss this.

Indemnity arrangements for a study need to be explained in the IRAS ethics application (Questions A76 and A77). RGIT can provide a standard statement if required.

4.2.2.3 Provide PI/CI with agreement for all Clinical Trials of Investigational Medicinal Products (CTIMPs)

Upon receipt of the items indicated in section 4.2.1, the RGIT will send the Chief Investigator an agreement (appendix 2) that must be fully signed prior to the study start, which will be checked and confirmed at the site initiation visit.

4.2.2.4 Agreement of Sponsorship

The Research Governance and Integrity Team will confirm Imperial College London or Imperial College Healthcare NHS Trust sponsorship to the Chief Investigator.

For Imperial College London sponsored projects this sponsorship will be confirmed to the CI by email and in writing via a signed letter. This will be accompanied by a copy of the Imperial College London insurance certificate for the study, for submission to HRA.

For Imperial College Healthcare NHS Trust sponsored projects, confirmation to the CI will be by email and letter only.

For studies occurring at ICHT, the relevant DRM will be copied into the sponsor letter. This is to facilitate liaison between the DRM and the study team for study CCC at ICHT.

The Research Integrity Officer and the Research Governance and Peer Review Officer will be copied into any sponsor letters for studies that have public database reporting requirements, so that RGIT can assist with registration and maintain oversight of reporting.

For all College sponsored studies involving personal data where the PI is based in the Faculty of Medicine (FoM), the FOM Data Protection Office will also be copied in to the sponsor letter by email to Faculty of Medicine GDPR Coordination. For the avoidance of doubt, personal data includes identifiable and pseudonymised (coded) data. The only time that the FoM DPO won't be copied in to a College sponsor letter will be if the study involves only the use of fully anonymised data (no link or code back to the patient).

The CI/study team must not assume that the College or ICHT will sponsor a project until written confirmation is received.

The email accompanying sponsor letter, Appendix 6 - RGIT_TEMP_057, must be read fully as it contains essential information relevant to the study being undertaken. This includes information on the online booking service, along with instructions to:

- Register any Faculty of Medicine (FOM) Imperial College London sponsored study using personal data on the FOM Asset Register
- Register any study requiring registration at clinicaltrials.gov as soon as possible by contacting the Research Integrity Officer.
- Register any study involving human tissue on DOCUMAS® by completing the DOCUMAS® Tissue Bank Tab for the end of the study, so that that tissue can be brought under the HTA licence as appropriate.
- Liaise with the Divisional Research Manager if the study is taking place at ICHT, to facilitate study set up and the CCC process, which must be confirmed before the study can start at ICHT.
- Send any updated documents where changes are requested by the REC, HRA, MHRA to the RGIT in order that RGIT has the most up to date versions of all study documents (also refer to section **4.4.2.1)**.
- Contact any external sites involved in the study to start the approvals process there. The study team should liaise with the relevant R&D departments according to HRA process.

When sponsorship is confirmed and the CI is ready to submit the project to the HRA, the Research Governance Manager , Clinical Trials Manager (CTM) or the Head of Research Governance and Integrity can sign the Sponsor Declaration or submit the study in CWOW IRAS

The sponsor representative should be copied into all approval letters by the REC/HRA/MHRA.

To facilitate set up of studies at ICHT, the RGIT will send the REC validation letter, provisional, conditional and favourable REC opinion letters (as applicable), HRA initial assessment letter (if received) and HRA approval letters to the DRM generic inbox. If the study was reviewed by the a Clinical Trials/Research Facilitator, they will responsible for forwarding these on to the DRM generic inbox when received via the RGM/CTM.

For studies with external sites, HRA process should be followed and the documents provided to the R&D offices by the study team.

For studies with non-NHS sites, the approval letters must be provided by the study team to the sites. Prior to study start up all approvals any contracts must be in place.

4.2.2.5 Continued review of sponsorship

The review of sponsorship is a continuous process and is dependent on the study having the appropriate approvals in place for the project to start up and for duration of the study.

If the required approvals are not in place for the start up duration of the study, RGIT can suspend sponsorship and inform the relevant regulatory bodies and ethics committees .

Sponsorship is also dependant on receipt of:

- all safety reports i.e. Development Safety Update Reports (DSURs) and Serious Unexpected Suspected Adverse Reactions (SUSARs), see RGIT_SOP_035
- any amendments to the study see RGIT_SOP_006;
- annual progress reports see RGIT_SOP_041
- End of study notification see RGIT_SOP_028.

4.3. LEGAL REPRESENTATIVE

The Legal Representative:

- Should be willing to act as the agent of the sponsor in the event of any legal proceedings instituted in the EEA (for example, for service of legal documents)

- Does not assume any of the legal liabilities of the sponsor(s) for the trial by virtue of the role of legal representative and does not therefore require insurance or indemnity to meet such liabilities, but may in some cases enter into specific contractual arrangements to undertake some or all of the statutory duties of the sponsor in relation to the trial, in which case the legal representative would also be regarded as a co-sponsor and would then require insurance or indemnity cover.

In all trials for which Imperial College London agrees to act as EU legal representative, a contract/written confirmation will be put in place with the sponsor to detail the responsibilities the College have agreed to undertake on behalf of the sponsor.

4.4. COMMUNICATION WITH SPONSOR'S REPRESENTATIVES

4.4.1 Sponsor's Representatives - Contacts

Once the study receives Imperial AHSC Sponsorship, the RGIT becomes the Sponsor's Representative for the duration of the study. This relevant person will be the Clinical Trial Manager for CTIMP studies and the Research Governance Manager for the Chief Investigator's campus or College site for non-CTIMP studies. See RGIT staff list.

4.4.2 Amendments

4.4.2.1 Amendments made to the study during the approvals process

Once the study has been submitted to the REC/HRA/MHRA (as applicable) changes to the documents may be requested during the approvals review process. Any amendments made during this time must come to the RGIT for their agreement of the changes, prior to resubmission. The updated documents should be sent for review with tracked changes to the CTM (for CTIMPs) and RGM (that is responsible for the Chief Investigator's campus or College site campus for non-CTIMP studies) who will then delegate to RGF's for review as deemed necessary.

4.4.2.2 Amendments made to the study following HRA approval for a study

All substantial and non-substantial amendments to study documentations must be reviewed and authorised by the RGIT prior to submitting them online to the HRA/REC and/or regulatory authorities (as applicable to the study).

The amended documents with the amendment tool should be emailed to the Sponsor's Representative for review, or submitted in CWOW IRAS which will be undertaken by the CTM/Clinical Trials Facilitator (CTIMP studies) or the RGM/RGF responsible for the Chief Investigator's campus or College site campus (for non-CTIMP studies). For detailed information, refer to RGIT_SOP_006 and RGIT_SOP_032.

The CTM/RGM/RGF reviewing the amendment will acknowledge its receipt review the changes within 5 working days of the receipt date.

Regulatory authorities will reject any amendments received without Sponsor's Representative authorisation (or authorised delegate from RGIT for minor amendments).

For all studies sponsored by the Imperial College AHSC and taking place at ICHT, the CTM/RGM/RF who has reviewed the amendment will forward all validation emails and approvals relating to the amendment to the DRM generic inbox. This is to facilitate communications between the study team and the DRM and the continuing CCC process for the amendment. For all other sites where the amendment will be implemented, IRAS guidance should be followed on the provision of amendment documents/approvals to sites and this will be the responsibility of the study team.

All required approvals/permissions must be in place before any amendment is implemented (HRA/REC/MHRA/CCC as applicable) as detailed in RGIT_SOP_006 and RGIT_SOP_032.

For College sponsored studies, if the amendment will have an impact on the GDPR aspects of the study the information provided on the FOM Asset Register must be updated by the study team before implementation of the amendment. If an amendment is being made and the study team have not yet registered the study on the FOM Asset Register, they will need to do this before implementation of the amendment.

It is advisable for the CI to inform the Sponsor's Representative of any communication with external parties, as some information may be privileged or may require contractual arrangements.

5. REFERENCES

UK Policy Framework for Health and Social Care Research (cited 15 June 2020)

HRA - Roles and responsibilities (cited on 15 June 2020)

EC Europa - DIRECTIVE 2001/20/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 4 April 2001 (cited on 15 June 2020)

Medicines for Human Use (Clinical Trials) Regulations 2004 (cited on 15 June 2020)

IRAS - Amendement guidance - all review bodies(cited 15 June 2020)

European Medicines Agency - ICH E6 (R2) Good clinical practice(cited on 15 June 2020)

HRA NHS Website (cited on 15 June 2020)

MHRA Good Clinical Practice guide Sixth Impression 2016

6. APPENDICES

The following Appendices list the following Templates associated to this SOP which can be found on the SOP, Associated Documents & Templates page.

Appendix 1: Guide to who should take on Sponsorship role

Who developed the project?	Source of Funding		The trial sponsor
	Trust	College	
College substantive employer and honorary contract with ICHT	Yes	No	ICHT
College substantive employer and honorary contract with ICHT	No	Yes	College
ICHT substantive employer and honorary contract with College	Yes	No	ICHT
ICHT substantive employer and honorary contract with College	No	Yes	College
Other Trust Employee *with* Honorary Contract at College (funds would go through College)	-	Funds go through College	College
Other Trust Employee *without* Honorary Contract at College	Funds go through Trust	No	ICHT
College substantive employer, honorary contract with ICHT or vice versa	Yes	Yes	Decision on IP rights and other factors.
College substantive employers and honorary contract with ICHT	No	No	College (but needs to be agreed with HOD prior to sponsor review being initiated)
ICHT substantive employers and honorary contract with College	No	No	ICHT (but needs to be agreed with DRM prior to sponsor review being initiated)

College – Imperial College London
ICHT – Imperial College Healthcare NHS Trust

Appendix 2: CI agreement for CTIMPs – RGIT_TEMP_019
Appendix 3: Risk Assessment Tool – RGIT_TEMP_020
Appendix 4: Sponsorship and Insurance Registration Form– RGIT_TEMP_021
Appendix 5: OID Contracts Flowchart (App.5) – RGIT_TEMP_022
Appendix 6: CTIMP Addendum Risk Assessment – RGIT_TEMP_054

Appendix 6: Sponsorship and Insurance Approval email – RGIT_TEMP_057
Appendix 7: Statistical Engagement Letter – RGIT_TEMP_058
Appendix 8: Process Map for OID and SoECATs – RGIT_TEMP_062