Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

Trinity College Dublin: Policy and Procedure for University Sponsorship of Regulated Clinical Trials

Version 4.0, 11Nov19

Version	Approval Status	Summary of Changes
Version 1.0	Working draft presented to Head of School of Medicine	New Document
Version 2.0	Trinity Research Committee: 26th April 2016 Trinity University Council: 11th May 2016 Trinity Board: 15th June 2016	Format change and finalised by the CRF working group
Version 3.0	Amended document for noting	• Amended to account for ICH GCP (E6) revision 2 addendum • Amended to reflect new role in the CRF to implement Sponsorship services (SPQM) • Format and content changed to align with status of document as a Trinity Policy • Reviewer (RDO, Contracts Office, SPQM) comments incorporated. • Application procedure split into two phases (pre- and post- grant approval) • Addition of a CRGG to assist in sponsorship oversight
Version 4		• Regulated Clinical trials added to the title of the policy • Amended QRAM to SPQM • CRF working group updates included • Amended Investigator Responsibilities • Definitions included for Trial Steering committee and Data and safety monitoring board • CRF abbreviation updated to SJH-CRF • Scope of the policy updated to reflect institutional changes • Regulatory framework updated to reflect changes and updates to regulatory framework • The Governance Model for Sponsorship in Trinity has been updated to reflect institutional changes • The roles and responsibilities for Sponsorship in Trinity has been updated • The application procedure for Investigators seeing sponsorship has been updated and the study registration form included in the appendix

		• The risk assessment and management sections have been updated as the information can be found in the quality management system and will be assessed on a case by case basis. • Withdrawal of Sponsorship has been updated to include additional information and clarification • Appendix 3 Job description has been removed to reflect institutional changes • Investigator Responsibilities have been updated to include additional clarifications • Title updated to include Regulated Clinical trials • Chief Investigator definition included

Table of Contents

1 Definitions

Term	Definition
1. Good Clinical Practice (GCP)	An international ethical and scientific quality standard provided by the International Council for Harmonisation for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials. It serves to protect the rights, integrity and confidentiality of trial subjects.
2. Funder	The organisation assessing the scientific quality of the research proposed and providing funding to facilitate the conduct of the proposed study, which then requires the Sponsor to takes responsibility before the Trial begins.
3. Health Products Regulatory Authority (HPRA)	Competent Authority in Ireland for regulating medicines, medical devices and other health products. This is the regulatory authority for clinical trials of IMPs and clinical investigations of medical devices.
4. Investigational Medicinal Product (IMP)	A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including a medicinal product that is already the subject of a marketing authorisation, but— a) is used, formulated or packaged in a way different from the form that is the subject of the authorisation, b) is used for an indication that is not included in the summary of product characteristics under the authorisation for the product, or c) is used to gain further information about the form of the product that is the subject of the authorisation An algorithm for determining whether or not a medicinal product is considered to be an IMP is provided in Appendix 1 of this policy and in cases of uncertainty, the HPRA should be contacted for guidance.
5. Medical Device (Definition as per Regulation EU 2017/ 745)	Any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes: — diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease, — diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability, — investigation, replacement or modification of the anatomy or of a physiological or pathological process or state, — providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations, and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.

6. Principal Investigator (PI)	The authorised health care professional (medical or dental) responsible for the conduct of a clinical trial at a trial site. If a trial is conducted by a team of authorised health care professionals at a trial site, the principal investigator (PI) is the leader responsible for that team. The PI is responsible for the day-to-day running or the study, overseeing the work of the study staff and the safety of study participants.
7. Chief Investigtor	A Chief Investigator in relation to a clinical trial conducted at a single trial site, is the investigator for that site. Where a clinical trial is conducted across several trial sites, the Chief Investigator is the authorised health professional, whether or not they are an investigator at any particular site, who takes primary responsibility for the conduct of the trial.
8. Site	The organisation providing access to the patient's/study subjects and retaining responsibility for the care of the participants to whom they have a duty of care (typically hospital site).
9. Sponsor	In relation to a clinical trial of an IMP the individual or organisation that takes responsibility for the initiation and management (or for arranging the initiation and management) of, and the financing (or arranging the financing) for that clinical trial (as per ICH E6) In relation to a clinical investigation of a medical device, the individual or organisation taking responsibility and liability for initiation or implementation of a clinical investigation (as per ISO 14155).
10. Third Party Vendor	A party that is sub-contracted to provide services to the sponsor to fulfil duties/ tasks required under Sponsorship
11. Trial Steering Committee	The role of the Trial Steering Committee (TSC) is to provide the overall supervision of the trial. Ideally, the TSC should include members who are independent of the investigators, their employing organisations, funders and sponsors. The TSC should monitor trial progress and conduct and advise on scientific credibility. The TSC will consider and act, as appropriate, upon the recommendations of the Data Monitoring Committee (DMC) or equivalent and ultimately carries the responsibility for deciding whether a trial needs to be stopped on grounds of safety or efficacy.
12. Data and Safety Monitoring Board/Data Monitoring Committee	A committee that may be established by the sponsor to assess at intervals, the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial.
Study Types	
13. Clinical Investigation (Medical Device)	A study undertaken to assess the safety or performance of a medical device in one or more human subjects that falls within the regulatory framework for medical devices, and therefore in Ireland, is regulated by the HPRA. Note that

	these regulations are distinct to, but in many areas overlap with, the regulations that govern IMP clinical trials. Studies of medical devices that are CE marked and used within their approved usage, generally fall outside of the scope of the regulatory framework and would be considered as non-regulated interventional research studies. Refer to section 6.1 for further information. Further guidance on the distinction between regulated and non-regulated medical device studies is available from the HPRA: http://www.hpra.ie/homepage/medical-devices/regulatory-information/clinical-investigations.
14. Clinical Trial (IMP) (also referred to as 'CTIMP')	Any investigation of an investigational medicinal product (IMP) in human subjects, other than a non-interventional trial (see definition below for this), intended: a) to discover or verify its clinical, pharmacological or other pharmacodynamic effects, or b) to identify any adverse reactions, or c) to study its absorption, distribution, metabolism and excretion, or to discover, verify, identify or study any combination of the matters referred to at subparagraphs (a), (b), and (c), with the object of ascertaining the safety or efficacy of such products, or both. Further guidance on the definition of a regulated clinical trial is available in Eudralex, Volume 10, Guidance Documents Applying to Clinical Trials, Questions and Answers, available on the website of the European Commission. In particular, the decision tree provided in the guidance is useful – a copy is included in Appendix 1 of this policy)
15. Non-Interventional Trial (as defined by SI 190 of 2004)	A study of one or more medicinal products which have a marketing authorisation, where the following conditions are met - a) the products are prescribed in the usual manner in accordance with the terms of that authorisation, b) the assignment of any patient involved in the study to a particular therapeutic strategy is not decided in advance by a clinical trial protocol but falls within current practice, c) the decision to prescribe a particular medicinal product is clearly separated from the decision to include the patient in the study, d) no diagnostic or monitoring procedures are applied to the patients included in the study, other than those which are ordinarily applied in the course of the particular therapeutic strategy in question, and e) epidemiological methods are to be used for the analysis of the data arising from the study;
16. Interventional Study	A clinical study in which participants are assigned to receive an intervention so that researchers can evaluate the effects of the intervention on biomedical or health related outcomes. This intervention could be of any type including, an investigational medicinal product, a prototype medical device, a nutritional supplement, a physiotherapy program or, as in Health Services Research, it could be the way in which services are configured or delivered. The trial could mandate that all the subjects receive the

	intervention of interest (a single arm trial) or that some subjects are randomly assigned to the intervention(s) of interest and others to a comparator – often a placebo- arm. *Note that these may also be referred to as 'clinical trials' in the scientific community, however, the Competent Authority (in Ireland the HPRA) uses the term "Clinical Trial" in a more restricted sense, in that they only apply it to Trials that fall under their jurisdiction (in general, trials of an Investigational Medicine Product or of a prototype medical device). The majority of clinicians/scientists who do not regularly interact with the HPRA may be confused by this this distinction.*
17. Regulated trial/ investigation	Interventional study (either a clinical trial of an IMP or a clinical investigation of a medical device) falling under the jurisdiction, by legislation, of the competent authority (in Ireland, the Health Products Regulatory Authority, HPRA)

2 Abbreviations

CA	Competent Authority
CE	Conformité Européene (European Conformity)
CI	Chief Investigator
CIS	Clinical Indemnity Scheme
HCSO	Head of Clinical Sponsorship Oversight
SPQM	Sponsorship Project and Quality Manager
SJH-CRF	Wellcome – HRB Clinical Research Facility at St James's Hospital
CRGG	Clinical Research Governance Group
EMA	European Medicines Agency
EU	European Union
EEA	European Economic Area
HSE	Health Service Executive
HRB	Health Research Board
HPRA	Health Products Regulatory Authority
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
PI	Principal Investigator
QMS	Quality Management System
RDO	Research Development Office, Trinity College Dublin
SOP	Standard Operating Procedure
SUSAR	Suspected unexpected serious adverse reaction
Trinity	Trinity College Dublin, the University of Dublin

3 Purpose of this Policy

The purpose of this policy is to provide clear guidelines for how Trinity College Dublin, the University of Dublin (Trinity) will take on the legal role of Sponsor for regulated clinical trials of investigational medicinal products and clinical investigations of medical devices [collectively referred to throughout this policy as "Clinical Trial(s)"] led by authorised academic investigators.

4 Scope of Policy

This policy applies to Sponsorship of regulated clinical trials of investigational medicinal products and clinical investigations of medical devices ("Clinical Trial(s)") led by authorised academic investigators.

- Trinity will only act as Clinical Trial Sponsor for Clinical Trials that have been approved following the review and application procedure outlined in Section 10 and where a written agreement to act as Clinical Trial Sponsor has been issued. The Clinical Trial Chief Investigator must be an employee of Trinity or have formal affiliation to Trinity.
- The operational costs of trial Sponsorship will be funded by the investigator.
- The SJH-CRF will provide operational support of Sponsorship services delegated by the Dean of Research until a Sponsorship Office is established in Trinity. Once this is established this document will be updated to reflect any changes. As part of the application process, applicants will need to confirm SJH-CRF resource availability to support the proposed Clinical Trial. All investigators are invited to contact the HCSO for assistance with estimating costs prior to submitting research grant applications.
- A review process (refer to section 10) will be used to determine suitability of each study for Sponsorship.
- The scope of services available through Trinity as Sponsor, is limited to those outlined in Appendix 2. Specific tasks outside this scope of services, such as IMP sourcing, unblinding service, data management or pharmacovigilance may need to be sub-contracted to an external vendor. This needs to be considered at grant application stage to be able to cost effectively for the trial. As Sponsor, Trinity is responsible for reviewing and approving any third-party vendors who are sub-contracted Sponsor tasks. Associated costs will be included in the Sponsor-investigator Agreement.

5 General Principles

5.1 Background

Under EU legislation, clinical trials of investigational medicinal products or clinical investigations of medical devices require a legal Sponsor to take responsibility for arranging the initiation, management and financing of the trial. Any legal entity (including a University) that is established in the EEA can act as Sponsor for such trials. The responsibilities of a trial Sponsor are defined in legislation and require extensive management oversight and governance. Clinical Trial Sponsorship by Trinity ("Trinity Sponsorship") allows investigators to apply for grant funding to undertake investigator-led Clinical trials.

5.2 Why Sponsorship Matters to Trinity

As a university, Trinity has a strong interest in ensuring it can serve as a Clinical Trial Sponsor to enable:

- Clinical research carried out in association with Trinity to be conducted according to the highest international standards for research governance, safety, integrity and transparency.
- Investigators to competitively pursue funding from Irish and EU sources for experimental medicine and clinical trials.
- Academic clinicians to undertake Clinical Trials that might not be undertaken by commercial pharmaceutical companies because of a lack of commercial incentives.
- Development of trial activity in the Trinity Cancer Institute.
- Trinity to raise its profile as a centre of research excellence.
- Institutional ownership of intellectual property

6 Regulatory Framework and Trial Sponsorship

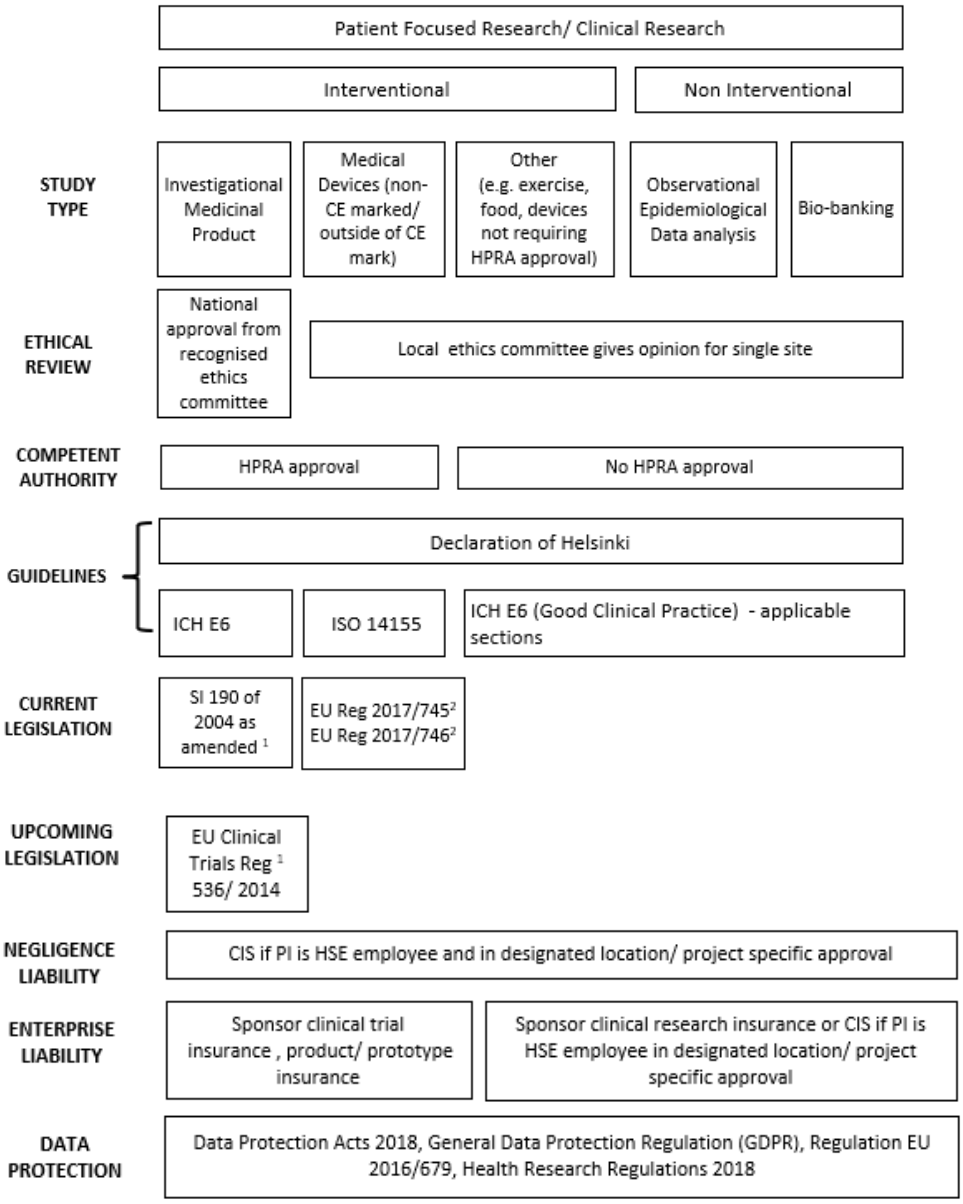
6.1 Overview of the Regulatory Framework for Clinical Research

Clinical research encompasses all health related research projects involving human participant contact, their tissue and/ or data. The regulatory and governance framework for clinical research in Ireland is summarised Figure 1.

Clinical trials involving IMPs or non-CE marked medical devices are governed by European and national legislation and require regulatory assessment and approval by a competent authority, which in Ireland is the HPRA (Health Products Regulatory Authority). The regulatry framework for IMP trials is outlined in figure 1. Any clinical trial of an IMP or a medical device falling within

the governance of the below legislation requires a legal Sponsor with responsiblities defined under legislation (refer to Section 8).

Figure 1 – Regulatory Framework for Clinical Research in Ireland



1. Clinical trial legislation: European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations, 2004, as amended by S.I. No 878 of 2004, S.I. No 374 of 2006 and S.I. No. 1 of 2009 to be superseded by the EU Clinical Trials Regulation 536/ 2014 in (anticipated) 2019

2. EU Regulation 2017/745 repealing Council Directives 90/385/EEC and 93/42/EEC with full implementation date of May 2020 and EU Regulation 2017/746 repealing Directive 98/79/EC with full implementation date of May 2022

7 Responsibilities of the Investigator Applying for Sponsorship

The Investigator must be a Trinity employee (or affiliated employee).

The Investigator has responsibility for the design, implementation, conduct and completion and management of the clinical trial and is accountable to Trinity (as Sponsor) in relation to the trial.

The investigator is required to submit an expression of interest to Trinity before submitting a grant application to enable adequate costing and feasibility review of Sponsorship prior to the grant application. The Investigator is required to complete a risk assessment and provide any requested supporting documents for review in a timely manner.

After funding has been granted a formal application can be made through the Clinical registration form (Appendix 3). The application will be reviewed in relation to but not limited to; accurate costing, risk mitigation plan, protocol development, resource identification, third party vendors and an implementation plan. It is the investigators responsibility to be forthcoming with this information and to update the sponsor should there be any changes.

The PI is responsible for the day-to-day running of the study and the safety of the study participants. This includes but is not limited to responsibility for overseeing the study budget, overseeing the work of study staff, ensuring that the study is conducted rigorously and on time and that all necessary regulations are complied with at all times. The PI must have training and certification in Good Clinical Practice (GCP) for the duration of the trial.

The PI is expected to ensure that:

- There are adequate funding and resources in place for running the trial
- The medical care of study participants is always assured
- Staff involved in the trial have appropriate Good Clinical Practice (GCP) training to fulfil their delegated activities
- Regular and timely communication is maintained throughout the trial to HPRA, HCSO and ethics committees
- There is full compliance to the protocol and that any deviations and/ or violations are documented and reported to the sponsor.
- Collection of accurate and high-quality data
- The trial complies with legal and ethical principles (as outlined in the Declaration of Helsinki)
- That records and reports are appropriately created, managed, stored and archived
- Serious adverse events are reported promptly and within 24 hours to the sponsor and Pharmacovigilance as per the Protocol and ICH- guidelines and applicable legislation.

8 Responsibilities of Trial Sponsors

The Clinical Trial sponsor is the legal entity that takes responsibility for the trial and for ensuring arrangements are in place to initiate and manage the study, including ensuring appropriate indemnity arrangements are in place for the study subjects as defined in ICH E6 or ISO 14155. The funder of the study is not necessarily the sponsor, e.g., where commercial companies fund the study they may or may not be the sponsor.

The duties and responsibilities of a Sponsor are detailed in ICH E6 GCP and a summary of this is provided in Table 1 (on the following page). Specific requirements for medical device trial Sponsors are detailed in ISO14155, but as there are considerable similarities between this and ICH E6, ICH E6 will be used as the reference throughout this policy.

The Sponsor is legally responsible for ensuring that the conduct of a trial and the final data it generates comply with all applicable legislation. There are clearly defined responsibilities of a Sponsor in the legislation, as detailed in Table 1.

8.1 Delegation of Sponsor Duties and Responsibilities by Trinity

Under legislation, Trinity as a Clinical Trial Sponsor may formally delegate by written agreement some, or all, of its trial-related Sponsor tasks to an individual (such as the investigator), institution or organisation. However, the ultimate responsibilty for the Clinical Trial and any delegated tasks still remains with Trinity as Sponsor. A delegation agreement will be put in place to indicate the distribution of Sponsorship tasks performed within the University, which will include the SJH-CRF and any delegation of Sponsorship tasks. Where agreed by the HPRA, certain responsibilties for Sponsor medical decisions on the trial may be delegated to the investigator

Table 1 - Overview of Sponsor Responsibilities as per ICH E6 (Good Clinical Practice Guidelines)

Quality Assurance and Quality Control • Implement a quality management system (risk-based) for all stages of the trial • Implement and maintain quality assurance and quality control systems with written standard operating procedures (SOPs) to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and regulatory requirements • Secure written agreement from all involved parties to ensure direct access to all source data/documents, and reports for the purpose of monitoring, auditing and inspection.
Competent Authority (HPRA) Approval and Research Ethics Committee opinion • Obtain HPRA approval to conduct the trial and ensure the investigator has obtained ethics approval for the conduct of the trial. • Submit all amendments for approval. • Submit annual updates and end of trial notification to the HPRA and ethics committees.
Trial Design and Statistical Analysis Ensure that qualified individuals (e.g. biostatisticians, clinical pharmacologists, and physicians) are used, throughout all stages of the trial process, from designing the protocol and case report (data collection) forms and planning the analyses to analysing and preparing interim and final clinical trial reports
Sub-Contracted Duties • Ensure that any delegation of duties to a third party such as a contract research organisation are transferred under written agreement • Maintain oversight and responsibility for any tasks delegated to a third party
Conduct and Management of clinical trial • Select the investigator(s) and institution(s) for conducting clinical trials • Ensure that conditions and principles of GCP are satisfied and adhered to • Ensure that the trial is conducted in accordance with the protocol, any subsequent amendments and conditions of authorisation • Provide appropriately qualified individuals to supervise the overall conduct of the trial, to handle the data, to verify the data, to conduct the statistical analyses, and to prepare the trial reports • Maintain and manage a trial master file to hold all documents relating to the trial • Medical expertise – designate qualified medical personnel for trial related medical queries • Establishment of independent data-monitoring committee (where appropriate) • Define, establish and allocate all trial related duties and functions
Pharmacovigilance • Ensure an Investigator Brochure exists and is reviewed and updated where necessary at least annually • Keep records of all adverse events reported by investigators • Record and report all suspected unexpected serious adverse reactions (SUSARs) in accordance with regulatory requirements and ensure investigators are informed of SUSARs

• Ensure all SUSARs are entered into the European Database • Provide an annual list of SUSARs and required safety reports to the CA and ethics committees • Establish systems for ongoing safety evaluation • Report all serious adverse events, serious adverse device effects (SADE) and any device deficiencies that could have led to a SADE to the ethics committee and/or regulatory authority
Monitoring and Auditing • Implementation of monitoring plan (risk-based) • Selection of monitors and provision of monitoring in accordance with the monitoring plan • Provision of risk-based auditing • Management of non-compliance
Data Handling and Record Keeping • Ensure that electronic data handling systems are validated against appropriate standards • Establish SOPs for use of electronic systems • Ensure data integrity • Maintenance and archiving of Sponsor essential documents and trial master file.
Manufacture, Importation and Labelling of Investigational Medicinal Product (IMP) • Meet all requirements for the authorisation to manufacture and import IMP • Ensure IMP has been certified by a Qualified Person (QP) • Ensure IMP is labelled in accordance with regulations
Indemnity • Provide indemnity and/or insurance to cover the liability of the investigator and the Sponsor
Contracts and Legal • Ensure contracts and/ or written agreements are in place for any duties delegated by the Sponsor and adequate oversight is maintained

* Where an agreement, such as a grant collaboration agreement, is already in place for a third party to perform Sponsorship tasks, Trinity as Sponsor will still need to perform a vendor review and approval procedure to ensure that delegated tasks are performed to an adequate standard.

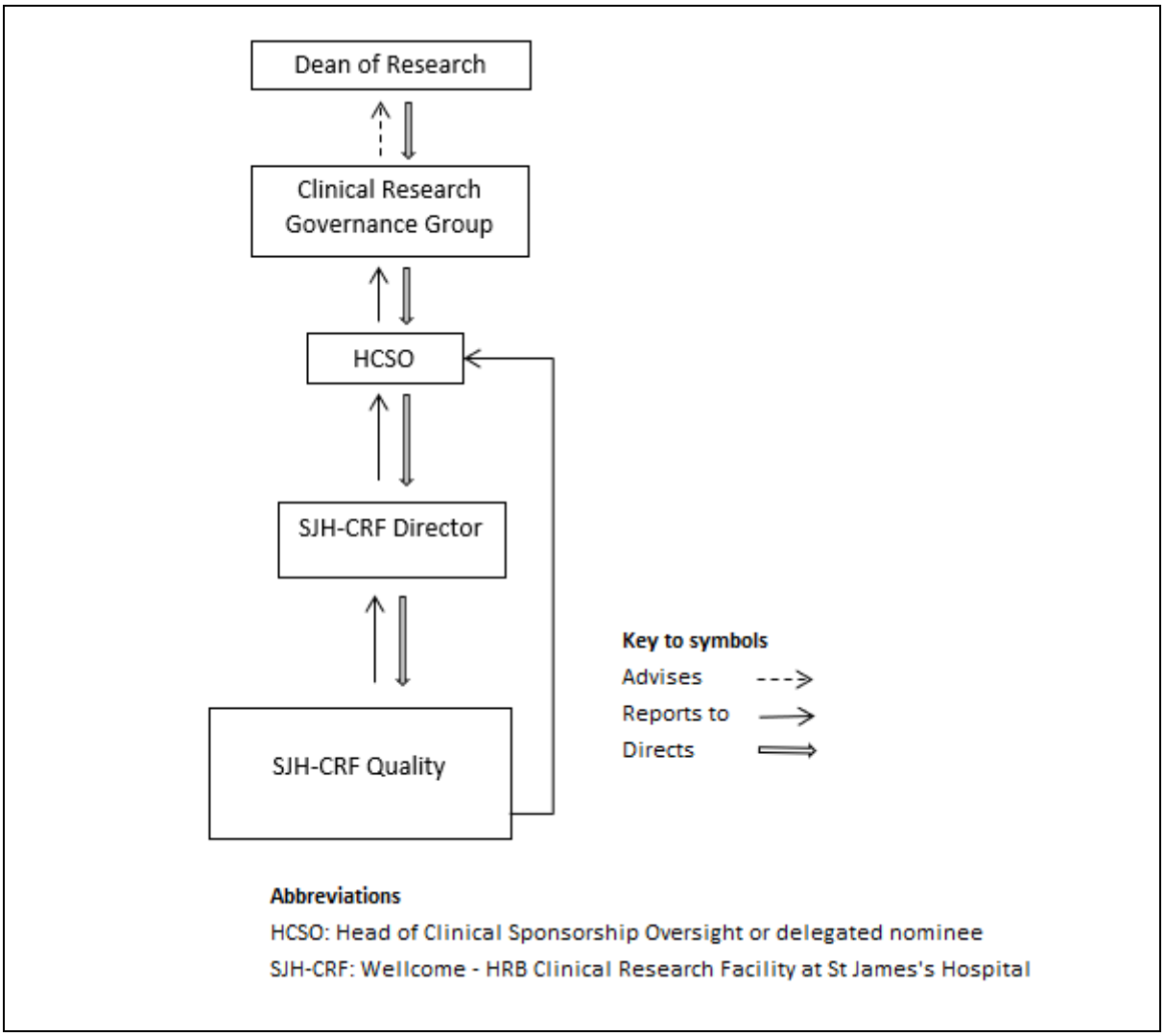
9 Governance of Sponsorship by Trinity

9.1 Governance

Within Trinity, Clinical Trial Sponsorship is overseen by the Dean of Research and managed by the Head of Clinical Sponsorship Oversight (HCSO). Operational support of Sponsorship can be provided by the Wellcome – HRB Clinical Research Facility located at St James's Hospital (SJH-CRF). The current model for governance of a regulated clinical trial Sponsorship within Trinity is as follows (illustrated in Figure 2):

- The Dean of Research is responsible for Clinical Trial Sponsorship on behalf of Trinity.
- The HCSO is responsible for operational oversight of Trinity Sponsorship.
- A Clinical Research Governance Group (CRGG) will be established in Trinity to advise the Dean of Research on trial Sponsorship decisions and to review risks associated with Sponsorship.
- A written clinical trial agreement (including delegation of agreed Sponsor tasks to PI) will be put in place between Trinity, the trial site and the PI.
- Distribution of Sponsor tasks within Trinity and to third parties will be described in a delegation agreement.
- The scope of services provided by the SJH-CRF to a Trinity sponsored trial will be agreed by the SJH-CRF Director.
- A trial steering committee and data and safety monitoring board will be established on a trial specific basis to ensure adequate review and oversight of the trial.

Figure 2 – Current Governance Model for a Regulated Clinical Trial Sponsored by Trinity



9.2 Roles and Responsibilities for Sponsorship in Trinity

9.2.1 Wellcome –HRB Clinical Research Facility at St James's Hospital (SJH-CRF)

The SJH-CRF was developed with the aid of a funding award made to the Trinity School of Medicine by Wellcome and the HRB and has been operated by Trinity since 2013. The SJH-CRF is located in St. James's Hospital and is jointly governed by St James's Hospital and Trinity.

The SJH-CRF employs a Quality Manager who is responsible for implementing a quality management system and operational procedures for Sponsor services.

A detailed matrix for execution of Sponsor-related tasks is provided in Appendix 2. This demonstrates the tasks that can be provided by Trinity and identifies functions that will need

to be provided by the Principal Investigator (PI) and their team or sub-contracted to external vendors.

9.2.2 Third Party Vendors

The SJH-CRF can provide operational support for regulatory and ethics submissions, trial monitoring, pharmacovigilance, site initiation, research nursing support, project management advice, a regulated trial site, lab, pharmacy services and assistance with selection of third-party vendors for IMP sourcing and data management. The investigator will be expected to take on responsibility for the protocol, trial organisation, data management, reporting functions, IMP sourcing, statistics and medical expertise. These activities will need to be performed in full accordance with ICH E6 (GCP) and relevant European and National legislation. On a case by case basis Trinity may delegate some of all sponsorship tasks to the Chief Investigator. This will be clearly outlined in the contract and agreements. Trinity will have overall responsibility and oversight of these tasks.

9.2.3 Head of Clinical Sponsorship Oversight (HCSO)

The HCSO is employed by Trinity to maintain operational oversight and coordination of Trinity Sponsorship. The HCSO provides, at application stage, assistance to PIs in design of protocol, establishing regulatory requirements, risk review and mitigation, trial costing and study set-up plan. Throughout the trial, the HCSO is reponsible on behalf of Trinity for maintaining oversight of operational conduct and ensuring that the trial is conducted in adherence with the agreed protocol and applicable legislation, safety reporting is conducted in adherence with legislative requirements, risk-benefit review is performed as per agreed protocol and non-adherence to the protocol is addressed with appropriate actions.

9.2.4 Research Development Office, Trinity Research and Innovation (RDO)

RDO is responsible for assisting investigators in applying for adequate funding to support Sponsorship and directing PIs to the SJH-CRF or HCSO for advice on applying for Trinity Sponsorship. All investigators are encouraged to contact the RDO for assistance with grant applications at the earliest stage possible to ensure that trials are adequately resourced at grant application stage.

9.2.5 Estates and Facilities

Estates and Facilities is responsible for ensuring that adequate insurance is maintained by Trinity to cover its obligations as Clinical Trial Sponsor. This includes indemnification of the

trial and trial protocol and where applicable, ensuring that prototype or product liability is in place. A questionnaire must be completed by the PI on application for Sponsorship to assist the insurance provider in confirming that scope of cover extends to the trial.

9.2.6 Contracts Office, Trinity Research and Innovation

The Contracts Office is responsible for ensuring that adequate agreements and contracts are in place to meet the responsibilities of Trinity as Sponsor, such as the clinical trial agreement with the trial site and investigator and any sub-contracted activities.

9.2.7 Clinical Trials Governance Group (CTGG)

A Clinical Research Governance Group will be established as an institutional committee responsible for ensuring that studies Sponsored by Trinity receive appropriate peer review and have adequate funding, resourcing, risk management and insurance cover prior to being accepted for Sponsorship. The CRGG will include members of staff in senior research management position with relevant experience in clinical research. The CRGG provides opinion to the Dean of Research on the suitability of a Clinical Trial for Sponsorship approval and maintains oversight of high-risk studies.

10 Application Procedure for Investigators Seeking Sponsorship

This section outlines the application procedure for Sponsorship.

10.1 Application Process

Expression of Interest/ Pre-Grant Funding:

The investigator makes an initial submission of Expression of Interest for Sponsorship to the RDO. The application process is as follows (illustrated in Figure 3):

1. PI submits and initial expression of interest to the RDO along with any study specific document such as the protocol.
2. The expression of interest along with the applicable documents are forwarded to the HCSO and SJH-CRF for review. Key criteria to be considered in the review are outlined in Section 10.2. The investigator will be asked to provide a detailed assessment of clinical risks.
3. The HCSO and SJH-CRF will liaise with the investigator to ensure that the protocol, resources, provisional quality management plan and cost estimate for grant submission is adequate and sufficiently informed for safe conduct of the trial. The following are examples of considerations at this stage:
    - Investigational medicinal product (IMP) sourcing

- Statistical design and analysis plan
- Risk-benefit review of the trial and procedures
- Risk management – monitoring and pharmacovigilance
- Data management and archiving
- Any requirement for expert opinion/ peer review
- Contractual issues/ IP
- Sub-contracted services (e.g. laboratory, pharmacovigilance, data management)
- Insurance requirement
- Project management
- Sponsor set up costs
- Monitoring and auditing

4. If the study is considered suitable for recommending for Sponsorship, the study will be referred onto the Clinical Trial Governance Group (CTGG) for a decision on whether or not Trinity will offer Sponsorship in principle. Please note that this is conditional and dependant on items such as; adequate funding, protocol review by Trinity, a risk-benefit review, a Trial Steering Committee and Data Monitoring Committee appointed, and formal approval process as outlined below.

Following Grant Funding Approval

5. The applicant submits a formal application of Sponsorship to the RDO (Appendix 3). This should be based on the protocol used in the initial Expression of Interest.
6. A detailed protocol review, Sponsorship project plan and accurate costing will be completed by the HCSO and SJH-CRF. This review is necessary to warrant that the university will take legal responsibility and provide appropriate insurance for the research proposed.

7. Where third party vendors will be required for a study, vendor quotes and selection process will be initiated.

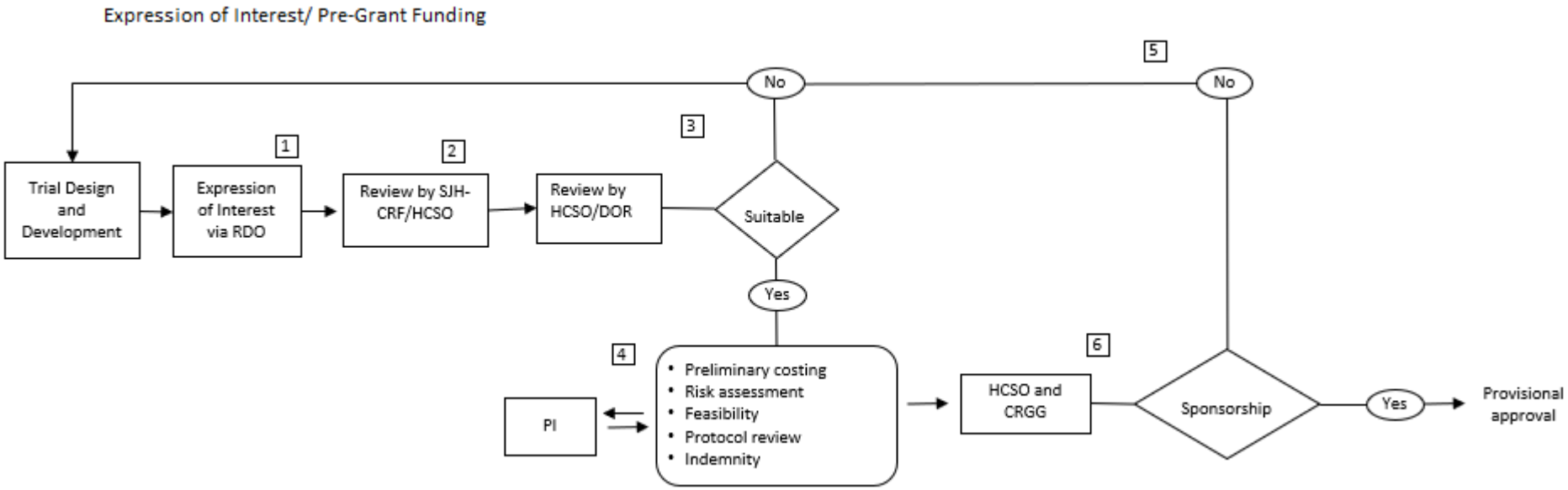
   The Dean of Research reviews the application with the recommendations of the Clinical Trial Governance Group and issues a formal decision on Trinity Sponsorship, including any additional conditions that might be required.
8. Contracts are finalised, a trial specific steering committee and data and safety monitoring board will be established by the HCSO or qualified designee. The trial set-up process commences as per the SJH-CRF SOPs and Quality Management System (QMS).

10.2 Key Assessment Criteria for Sponsorship

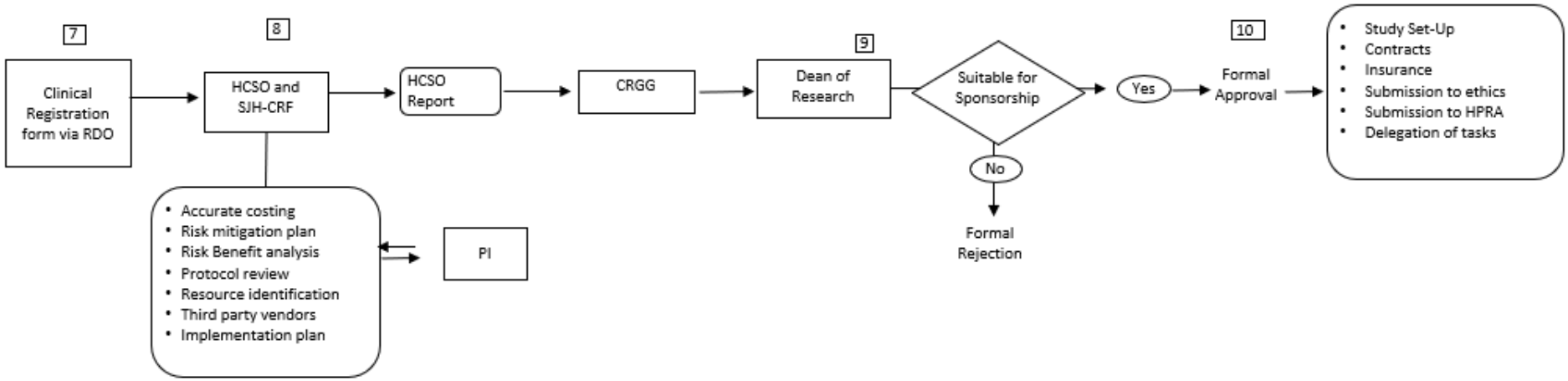
There are a number of areas that will be taken into consideration when assessing a study for Sponsorship suitability. These include but are not limited to:

1) Trial risks
2) Scientific or clinical justification
3) Investigator (and team) experience
4) Project feasibility
5) Strategic alignment
6) Adequate funding and resourcing for Sponsorship

Figure 3: Proposed Process for Application to Trinity for Sponsorship



Formal Application/ Post-Funding



Abbreviations

HCSO: Head of Clinical Sponsorship Oversight or delegated nominee

SJH-CRF: Wellcome - HRB Clinical Research Facility at St James's Hospital

11 Risk Assessment and Management

All clinical research involves potential risk to the research subject, PI, Sponsor and funder. Trinity will implement a risk assessment and management plan to ensure that risks associated with Trinity Sponsored trials are appropriately mitigated. This requires stringent application review and trial management processes that are rigorous, reliable, transparent, quantifiable and auditable.

11.1 Types of Risk Associated with Clinical Research

In patient focused research risks may arise from a variety of sources but these are usually predictable. Understanding the origins of research risk is important if such risks are to be properly assessed and managed. Potential sources of risk include but are not limited to:

- **Phase of trial/ available clinical data –** the level of risk will depend on how much is known about the IMP or the device, for example there is less information available on potential risks associated with a phase I or first-in-human study than a phase IV trial or a trial using a marketed product.
- **Nature of intervention –** the type of medical device (example, class III surgically implanted device versus class I device) or pharmacological properties of the IMP will have a significant impact on the risk level of the trial.
- **Study population** – the level of risk varies with specific research population and levels of comorbidity. For example, it will often be higher in studies involving pregnant women and young children or people with chronic diseases such as diabetes.
- **Study Procedures** –the study procedures and trial design will impact on the level of risk. Non-routine clinical procedures will provide a source of additional risk as will study design, such as complex randomisation or blinding procedures.
- **Research team** – where the expertise and experience of the team members and the resources they have at their disposal affects the risk of a study
- **Conflicts of interest**: may be a risk factor, for example, if the investigator leading the study has a vested interest in the study demonstrating efficacy.
- **Data Protection**: a data privacy impact assessment will be required as part of study design to ensure that risks are identified and measures, including training, are adequate to ensure data privacy.

11.2 Assessment of Risk

All applications for Trinity sponsorship will undergo a risk assessment as outlined in appendix 4. This assesses the level of risk (high, medium, low), considers the probability of a risk being realised and includes the controls to mitigate the risk. The Sponsorship Risk Assessment form (Appendix 4) should be completed by the PI and the HCSO or designee and will be submitted with the application for sponsorship.

11.3 Risk Management Plan

Risk management does not eliminate risk, but it can reduce risk and reduce the impact of risks. A risk management plan will be implemented to minimise risks for the life-cycle of a trial. This will be based on the trial protocol review and Sponsorship Risk Assessment Form. Risks will be reported, and issue escalated as per the SJH-CRF SOPs and quality management system.

11.4 Quality Management System

A robust Quality Management System with specific standards for each clinical trial is important to meet regulatory expectations and to assess and mitigate against risk. Quality of clinical trials depends on data integrity and participant protection. The Quality Management Systems will include but is not limited to: personnel roles and responsibilities, training, policies and procedures, quality assurance and auditing, document management, record retention, risk assessment and management, reporting and corrective and preventive action. Trinity sponsored clinical trials will adhere to the Quality Management system of the SJH-CRF.

12 Withdrawal of Sponsorship

Trinity has the discretion to withdraw Sponsorship of a trial where information provided on the original application changes without prior notification to the HCSO and approval of the Dean of Research. This includes, but is not limited to:

- Principal investigator
- Site deficiencies
- Inadequate Funding
- Trial design
- Risk based review
- Risk Benefit analysis

Sponsorship may also be withdrawn if there is failure to comply with legislation, conditions of approval, study protocol or risk management plans.

13 Insurance

Trinity as Sponsor must ensure that there is appropriate insurance cover in place for:

- the study subjects
- those involved in conducting the research
- Trinity.

Trinity has a clinical trials insurance policy in place. There are some exemptions and limitations to the scope of research covered under the policy. Insurance cover for the trial and any prototype or novel product will need to be confirmed as part of the application review process and the PI may be asked to provide additional funding to extend cover where necessary.

Medical Malpractice

Medical practitioners practising in public hospitals in Ireland are covered by the national Clinical Indemnity Scheme (CIS), which is administrated by the State Claims Agency. This is essentially a state insurance scheme covering clinical practitioners working in public hospitals. The scheme compensates patients who may have been harmed in a public hospital. All hospital sites will be required to confirm medical malpractice/ negligence cover is in place and extends to clinical trials before the study start.

While the scheme covers medical negligence that may occur during the course of a trial, it doesn't cover incidents arising from the trial itself, or poor trial design. This cover extends to the PI and the staff working on the study under the direction of the PI.

Appendix 1: Decision Tree to Establish Whether a Trial is a 'Clinical Trial'

This algorithm and its endnotes will help you answer that question. Please start in column A and follow the instructions. Additional information is provided in the notes at the end of the table. If you have doubts about the answer to any of the questions contact the clinical trials unit of your competent authority.

A	B	C	D	E
A CLINICAL TRIAL OF A MEDICINAL PRODUCT?				A NON-INTERVENTIONAL CLINICAL TRIAL?
Is it a medicinal product (MP)?[i]	Is it not a medicinal product?	What effects of the medicine are you looking for?	Why are you looking for those effects?	How are you looking for those effects?
If you answer no to all the questions in column A, the activity is not a clinical trial on a MP. If you answer yes to any of the questions below go to column B.	If you answer yes to the question below in column B the activity is not a clinical trial on a MP. If you answer no to this question below go to column C.	If you answer no to all the questions in column C the activity is not a clinical trial under the scope of Directive 2001/20/EC. If you answer yes to <u>any</u> of the questions below go to column D.	If you answer no to <u>all</u> the questions in column D the activity is not a clinical trial under the scope of Directive 2001/20/EC. If you answer yes to any of the questions below go to column E.	If you answer yes to all these questions the activity is a non-interventional trial which is outside the scope of Directive 2001/20/EC. If your answers in columns A,B,C & D brought you to column E and you answer no to any of these questions the activity is a clinical trial within the scope of the Directive.
A.1. Is it a substance[ii] or combination of substances presented as having properties for treating or preventing disease in human beings? A.2. Does the substance function as a medicine? i.e. can it be administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action or to making a medical diagnosis or is otherwise	B.1. Are you only administering any of the following substances? • Human whole blood[iii]; • Human blood cells; • Human plasma; • A food product[iv] (including dietary supplements) not presented as a medicine; • A cosmetic product[v] • A medical device	C.1. To discover or verify/compare its clinical effects? C.2. To discover or verify/compare its pharmacological effects, e.g. pharmacodynamics? C.3. To identify or verify/compare its adverse reactions? C.4. To study or verify/compare its pharmacokinetics, e.g., absorption, distribution, metabolism or excretion?	D.1. To ascertain or verify/compare the efficacy[vi] of the medicine? D.2. To ascertain or verify/compare the safety of the medicine?	E.1. Is this a study of one or more medicinal products, which have a marketing authorisation in the Member State concerned? E.2. Are the products prescribed in the usual manner in accordance with the terms of that authorisation? E.3. Does the assignment of any patient involved in the study to a particular therapeutic strategy fall within current practice and is not decided in advance by a clinical trial protocol[vii]? E.4. Is the decision to prescribe a particular medicinal product clearly

administered for a medicinal purpose? A.3.Is it an active substance in a pharmaceutical form?				separated from the decision to include the patient in the study? E.5. Will no diagnostic or monitoring procedures be applied to the patients included in the study, other than those which are applied in the course of current practice? E.6. Will epidemiological methods be used for the analysis of the data arising from the study?

[i] Article 1(2) of Directive 2001/83/EC, as amended.

[ii] Substance is any matter irrespective of origin e.g. human, animal, vegetable or chemical that is being administered to a human being.

[iii] This does not include derivatives of human whole blood, human blood cells and human plasma that involve a manufacturing process.

[iv] Any ingested product which is not a medicine is regarded as a food. A food is unlikely to be classified as a medicine unless it contains one or more ingredients generally regarded as medicinal and indicative of a medicinal purpose.

[v] The Cosmetic Directive 76/768/EC, as amended harmonises the requirements for cosmetics in the European Community. A "cosmetic product "means any substance or preparation intended for placing in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and mucous membranes of the oral cavity with the view exclusively or principally to cleaning them, perfuming them or protecting them in order to keep them in good condition, change their appearance or correct body odours.

[vi] Efficacy is the concept of demonstrating scientifically whether and to what extent a medicine is capable of diagnosing, preventing or treating a disease and derives from EU pharmaceutical legislation.

[vii] Assignment of patients to a treatment group by randomisation planned by a clinical trial protocol cannot be considered as current practice.

Reference: Eudralex, Volume 10, Guidance Documents Applying to Clinical Trials, Questions and Answers available on the website of the European Commission. This is applicable to trials falling within the scope of Directive 2001/20/EC. This will be replaced and new guidance issued in 2019 when EU Clinical Trials Regulation (536/2014) comes into effect.

Appendix 2: Detailed Delegation of Sponsorship Tasks – Scope of Services

PI	Principal Investigator	CO	Contracts Office, Trinity Research and Innovation
HCSO	Head of Clinical Sponsorship Office	DOR	Dean of Research
SJH-CRF	Clinical Research Facility (this includes the SPQM)	E&F	Estates and Facilities
Third Party	Third party service provider may be required - funding provided by PI/ study		

TASK	**PI**	**SJH-CRF**	**HCSO**	**CO**	**E&F**	**Third Party**	**DOR**
Implementing and maintaining quality assurance and quality control systems with written SOPs in compliance with protocol, GCP and regulatory requirements		x	x				
Review study specific SOPS	x	x	x				
Quality control system for data handling		x				x	
Organise external independent audit			x				
Review of audit			x				
Escalation of non-compliance			x				x
Securing agreements to ensure direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring, auditing and inspection				x			
Obtain agreement (written) from investigator to comply with GCP, applicable regulatory requirements and approved protocol and to permit monitoring, audit and inspection.				x			
Study related contracts put in place				x			
Ensuring appropriate written agreements are in place for all sub-contracted responsibilities				x			
Define, establish, and allocate all trial-related duties and functions		x	x				
Maintain delegation log		x	x				
Provision of suitably qualified medical personnel	x						
Selection of investigator(s)/institution(s).	x		x				x
The Sponsor should utilise qualified individuals (e.g. biostatisticians, clinical pharmacologists, and physicians) as appropriate, throughout all stages of the trial process, from designing the protocol and CRFs and planning the analyses to analysing and preparing interim and final clinical trial reports.	x					x	

TASK	PI	SJH-CRF	HCSO	CO	E&F	Third Party	DOR
Selection of investigator(s)/institution(s).	x		x				x
Provision of protocol and an up-to-date Investigator's Brochure to investigator/institution.	x						
Preparation, approval and submission of EC application and amendments	x	x					
Response to EC questions	x	x					
Retain copy of EC approval documents		x					
Preparation, approval and submission of CA/ HPRA applications and amendments	x	x					
Response to CA/ HPRA questions	x	x					
Retain copy of CA/ HPRA approval documents		x					
Investigator's brochure and changes or annual updates	x						
Manufacture, labelling and packaging (if required) and changes to manufacture						x	
Obtaining importation/ manufacturing licences	x					x	
Obtaining/ contracting QP release documents	x	x					
Retaining copies of importation/ manufacturing/ export licences		x					
Randomisation code generation and quality control	x	x				x	
Unblinding procedure	x	x				x	
IMP stability testing and IMP sample retention						x	
Product distribution to investigator						x	
Control of receipt of IMP		x					
Storage and handling instructions for IMP		x					
Accountability log for IMP		x					
Recall procedures for IMP		x				x	
Destruction of unused IMP		x				x	
Records for IMP: shipment, receipt, storage, disposition, return and destruction		x					
Selection and qualifications of study staff	x	x					
SOP for monitoring		x	x				
Preparation of monitor plan		x					
Review of monitor report			x				

TASK	PI	SJH-CRF	HCSO	CO	E&F	Third Party	DOR
Escalation of significant issues			x				x
Review of deviations		x	x				x
The Sponsor may consider an independent data-monitoring committee to assess the progress of a clinical trial, including the safety data and the critical efficacy.			x				x
Ongoing safety evaluation	x		x				x
Notification of ongoing safety measures to CA/ HPRA, ethics committee and PI	x	x					
Implementation of urgent safety measures	x		x				
Submission of safety updates to CA/ HPRA	x	x					
Unblinding and medical cover	x						
Staff training	x	x					
Maintain trial master file		x					
Case report form creation, review and approval	x	x				x	
System suitability check		x					
SOP for electronic data processing system		x				x	
Data entry, review and processing	x	x					
Maintain a security system that prevents unauthorized access to the data						x	
Data backup						x	
Safeguard of blinding during data processing		x				x	
Documented list of individuals with permission to make data changes		x					
Statistical analysis	x					x	
Quality control check of trial master file		x					
Clinical study report submission to CA/ HPRA	x	x					
Archiving of trial documents	x	x					
Provision of insurance and indemnity to cover the PI and institution against claims arising from the trial including malpractice and negligence	x				x		
Provision of treatment costs for trial subjects in the event of trial related injuries					x		

Appendix 3: Clinical Study Registration Form

CLINICAL STUDY REGISTRATION FORM ***Please place an X where appropriate***	
Chief Investigator (CI) Contact Details	
Name:	
CI's employer(s):	
Department:	
Email:	Telephone:
Clarify if the CI is a: HSE employee ☐ Academic institution employee ☐ Joint academic institution/HSE joint employee ☐	
Your Contact Details (Please complete only if you are not the CI)	
Name:	
Your employer(s):	
Department:	
Email:	Telephone:
If you are an employee of the HSE/voluntary hospital only, please clarify your affiliation with the academic institution:	
Project Details	
Brief Summary of the Proposed Study– attach separate sheet if necessary *(Include details of study methodology and any clinical procedures participants will undergo including any diagnostics interventions (for example imaging)).*	
Nature/type of intervention:	
Start date:	**End date:**
Category: Non-interventional ☐ Interventional ☐ If interventional, please state type of intervention:	

Type of study: Investigational Medicinal Product study ☐ Medical device study ☐ Other ☐ Please specify:
Does this study require HPRA approval? Yes ☐ No ☐ Unsure ☐ Please specify:
Location of Research - list all locations where the study will be carried out (in academic institution, hospital, primary care locations)
Will the study be run in conjunction with the clinical research facility (CRF/)?
Where will research take place? Please specify locations.
Is this a multi-site study? Yes ☐ No ☐
Funding
Is there planning funding for this study: Yes ☐ No ☐
External funding source: Yes ☐ No ☐ If yes, please specify the grant holder
Internal funding source: Yes ☐ No ☐ If yes, please specify
Parties Involved in the Study and their Role
Please clarify which party is writing/designing the protocol:
Please clarify which party is to assume the role of the Sponsor:
Name of personnel working on the study and identify who is leading the study:
Is there any other external/third party providing financial, in-kind or other support for the study? Yes ☐ No ☐
If yes, clarify their role (for example providing free products):
Please clarify which party shall have the commercialisation rights (if any):
Participant Information
Participant Type:

Anticipated Number of Participants:
Will your research involve: Pregnant women ☐ Children under 16 ☐ Genetic engineering ☐ Contraceptives ☐ Administration or use of medicinal substances, devices or equipment manufactured by the academic institution ☐
Will any of the research participants have the following conditions: HIV ☐ Hepatitis ☐ CJD ☐
Involvement of Academic Institution Employees in the Study
Will the study involve academic institution employees: Yes ☐ No ☐
If yes, please specify role of the academic institution employees (select from one or more from the following options) Obtaining patient consent ☐ Collection of phenotypic data ☐ Collection of clinical samples ☐ Other ☐ Please clarify**:**
If clinical samples are collected, please clarify what will be collected and where this will occur:
Will the study involve diagnostic interventions: Yes ☐ No ☐ If yes please specify what, by whom and where this diagnostic intervention will occur:
Additional Details
Are there any other factors that should be highlighted at this point so that they can be brought to the insurer's attention and can be used in consideration for the Sponsor Office(r) risk assessment of the proposal? If so, please specify.

CHIEF INVESTIGATOR:	_____ **PRINT NAME** _____ _____ **SIGNATURE** **DATE**

To be completed by Sponsor designee
Review date:
Study's reference number:
Preliminary risk classification: Low ☐ Medium ☐ High ☐
Insurance Study fall under general policy ☐ Study requires additional premium ☐ Specify amount €: Study cannot be insured ☐ SCA approval ☐
Outcome of preliminary risk assessment Study can proceed ☐
Study can proceed, subject to specific requirements being met ☐ Requirements:
Study is subject to sponsorship risk assessment and approval ☐
Study cannot proceed ☐
Sponsor review completed by:

Name:	
Signature:	
Date	

Appendix 4: Sponsorship Risk Assessment Form

SPONSORSHIP RISK ASSESSMENT FORM
• *This form should be completed by the chief investigator (CI) and the Sponsor Office(r) (SO) (or nominee/equivalent).* • *Where applicable please include exact reference to the document (e.g. protocol) and page number where more information on the information provided can be found.*
Study Application reference number:
CI's name:
Title of proposed trial:
Short title:
Primary trial objective(s):
Secondary trial objective(s):
Trial Classification: Non-interventional - observational ☐ Interventional – non-regulated ☐ Interventional regulated ☐
Trial Phase:
Trial Design and Complexity: *(indicate all that apply)* Open label ☐ Placebo controlled ☐ Randomised – indicate no of trial arms ☐ Blinded ☐ Cross over ☐ Other ☐ specify design (e.g. 2x2 factorial):
Trial Participants: (indicate all that apply) Healthy volunteers ☐ Patients ☐ Patients with poor prognosis/terminal disease ☐ Patients in emergency situations (e.g. unconscious) ☐ Patients incapable of giving consent personally ☐ Children under 5 years of age ☐ Children between 5 -16 years of age ☐ Women of childbearing potential (no contraception requirement in protocol) ☐ Pregnant or nursing women ☐ Other – specify:
Trial Size and Sites:
Total Anticipated Number of Patients:
Statistical Rationale for the Anticipated Number of Patients:

Estimated Recruitment Period for all Patients: (months/years)

Estimated Duration of Clinical Visit Phase: (months /years)
(i.e. taking the FPFV and LPLV timeline into consideration)

Estimated Set-Out and Close Out Duration: (months)

Total Duration of the Trial

- **Treatment duration per patient (e.g. single administration, or administrations over X number days/weeks/months):**
- **Follow-up period per patient (e.g. number of weeks, months, years):**

Number of Sites:
One ☐ Multiple ☐
If multiple, provide information below as applicable
Number of ROI Sites:
Number of EU Sites:
Number of Non-EU Sites:

Details of all proposed sites: *public/private refers to whether the hospital/clinic is a public hospital (i.e. HSE, NHS etc), or private entity.

Site	Address	*Public/Private	PI

Risks Identified:

Risk Level: Low ☐ Medium ☐ High ☐

Mitigation Plan:

How is the trial being funded? *(Check more than one box if multiple sources of funding apply)*
Commercial source ☐ Public or charity funded ☐

In-house funds, specify the account details:

Has funding already been secured for the trial? Yes ☐ No ☐

If yes, please provide the details of funding received (i.e. copy of any award letter(s) and a breakdown of funding provided)

If no, please clarify funding plan

Is the trial budget (secured or planned) sufficient to cover all the costs of the trial?
Yes ☐ No ☐

If it is not sufficient, please clarify
(budget required for sponsorship approval)

Funding Risks Identified:

Risk Level: Low ☐ Medium ☐ High ☐

Mitigation Plan:

Training and experience

Has the CI adequate GCP training? Yes ☐ No ☐
If no, green light will be subject to confirmation of adequate GCP training

Has the chief investigator suitable experience?

(a) in the therapeutic area of the proposed study? Yes ☐ No ☐
(b) in conducting the type of study that is proposed? Yes ☐ No ☐
(c) in use of the IMP (or trial procedures in the case of a surgical intervention)? Yes ☐ No ☐

Will the study operational team and all individuals who will interact with patients in the course of performing their role in the study trained in GCP?
Yes ☐ No ☐

Additional information:

Risks Identified:

Risk Level: Low ☐ Medium ☐ High ☐

Mitigation Plan:

For randomised trials only

Have randomisation personnel/systems already been identified?
No ☐ Yes ☐

If yes, please specify:

Is it already known who will assign the treatment allocations?

No ☐ Yes ☐

If yes, please specify:

Is the treatment blinded? No ☐ Yes ☐
If yes, please specify:

Risks Identified:

Risk Level: Low ☐ Medium ☐ High ☐

Mitigation Plan:

Information about the IMP

Product name:
Dose:
Name of active substance:
Pharmaceutical Form: Tablet / Capsule ☐ Powder for Reconstitution ☐
Other ☐
Please specify:

Type of IMP
a) Biological or biotechnological product Yes ☐ No ☐
b) Advanced therapy medicinal product Yes ☐ No ☐
c) IMP classified as genetically modified organism (GMO) Yes ☐ No ☐
d) IMP consisting of tissues or cells Yes ☐ No ☐

Route of administration:
Generic product to be used: ☐
Specific brand to be used Specify manufacturer: ☐

Does the IMP have a marketing authorisation in the ROI?
Yes ☐ No ☐ N/A (Placebo) ☐
If no, in which country is the IMP licensed:

Is the IMP to be used (dose and route of administration) within its licensed indication as per the summary of product characteristics (SmPc)?
Yes ☐ No ☐
If no, please provide further details and rational

Is the IMP to be used in the same patient population as per the SmPc?
Yes ☐ No ☐

If no, please provide further details and the rational

Will IMP be used in its marketed form? (i.e. no further manufacturing required e.g. radio labelling, over encapsulation)
Yes ☐ No ☐
If no, please provide further details and rational

How will the IMP be stored?
as per SmPC ☐
Other, please provide further details and rational

Risks Identified:

Risk Level: Low ☐ Medium ☐ High ☐

Mitigation Plan:

Source of Treatment (IMP including Placebo)
N/A if no IMP ☐ N/A Hospital stock will be use, subject to budget being agreed with hospital pharmacy) ☐
If NA, skip this section

Is a pharmaceutical company supplying the IMP? No ☐ Yes ☐
if yes please provide name of company and associated costs

Will the IMP be sourced from a wholesaler? No ☐ Yes ☐
If yes please provide name of wholesaler:

Does the IMP have a marketing authorisation in the ROI? Yes ☐ No ☐ N/A (Placebo) ☐
If no, in which country is the IMP licensed?

Will IMP be sourced in the ROI? Yes ☐ No ☐
If 'No'
Where will IMP be sourced?

Has an importer been identified? No ☐ Yes ☐
If yes, please provide details:

Does the IMP require specific manufacturing (e.g. placebo, over encapsulation, etc) for this trial?
No ☐ Yes ☐

If yes, please complete section 10.5.1 and 10.5.2 below

Name of manufacturer:

Active pharmaceutical ingredient and source:

If the IMP is not supplied by a pharmaceutical company or a wholesaler, please specify where and how the IMP will be sourced for the trial:

Has negotiation with the manufacturer/importer/ supplier been initiated?
Yes ☐ No ☐ NA ☐

Risks Identified:

Risk Level: Low ☐ Medium ☐ High ☐

Mitigation Plan:

Non-Investigational Medicinal Products (NIMPs)
Please list all known NIMPs (Non-Investigational Medicinal Products, such as rescue medication, background treatment):

	NIMP	**Proposed Dose** (including units)	**Route of administration**	**Frequency & Total Duration**
1.				
2.				
3.				
4.				
5.				
6.				

Device details
Product Name:
Manufacturer's name:
Manufacturer's address:

Device Classification Class I ☐ Class IIa ☐ Class IIb ☐ Class III ☐
Does the device have CE marked approval? Yes ☐ No ☐

If 'Yes' does the study plan to use the device within its existing intended purpose and indications for use? Yes ☐ No ☐

If 'No' and the device will be used outside the terms of its existing CE mark e.g. 'off-label' provide detail on the off-label use:

Has the HPRA being engaged in discussions on off-label use and requirement for regulatory oversight of the investigation?
Yes ☐ No ☐

Risks Identified:

Risk Level: Low ☐ Medium ☐ High ☐

Mitigation Plan:

Manufacturer of the device
Applicable ☐ N/A ☐
If N/A:

Is a commercial company supplying the device? No ☐ Yes ☐
If yes please provide name of company and associated costs

If applicable:
Will the device be sourced in the ROI? Yes ☐ No ☐

If 'No', where will device be sourced?

Has an importer been identified? No ☐ Yes ☐
If yes, please provide details:

Does the device require any design alterations for this trial? Yes ☐ No ☐
Name of manufacturer

Name responsible person to ensure min. essential requirement conformation prior to investigation initiation:

Does the device require ancillary reagents or consumables? Yes ☐ No ☐
If yes, outline ancillary reagent details, manufacturer and marketed status:

Ancillary reagent name: **Ancillary reagent supplier and marketed status:**
Risks Identified:
Risk Level: Low ☐ Medium ☐ High ☐
Mitigation Plan:
Managing adverse events and serious adverse events: Has appropriate consideration been given to potential adverse events and serious adverse events that may arise in the course of the study and are appropriate organisational structures in place to ensure appropriate response and management of same (e.g. Sponsor oversight management)? Yes ☐ No ☐ **Additional information:**
Division of Responsibilities Are the responsibilities of institutions involved in the study (e.g. academic institution, clinical site(s), industry partner, other) clearly identified and appropriately allocated? *(please enclose division of responsibilities table in the documentation for SOC)* Yes ☐ No ☐ **Additional information:** **Does the chief investigator understand and accepts his/her responsibilities?** Yes ☐ No ☐ **Additional information:**
Independent Data Monitoring Committee (IDMC) Is an IDMC required for the study and have arrangements been made? Yes ☐ No ☐ **Additional information:**
Sample collection and storage arrangements Are appropriate collection and storage arrangements in place to ensure the integrity of samples collected in the course of the study? Yes ☐ No ☐ **Has a trial statistician been identified?** Yes ☐ No ☐ **Name and institution of the trial statistician:** **Additional information:**
General Data Protection Regulation (GDPR) Are appropriate mechanisms in place to ensure data is securely stored and managed in accordance with GDPR? Yes ☐ No ☐ **If no, clarify:**

Note: Data protection impact assessment and management plan are required for sponsorship approval

Conflict of Interest *(Complete this section considering all parties involved in the trial)*

	Yes	No	N/A
Is the CI being paid directly by any commercial party to participate in the trial?			
Do any of the commercial parties involved in the trial plan to use the trial data for purposes of licensing the IMP/device or varying the current marketing authorisation?			
Does the CI occupy a position of director, partner, consultant or trustee in any of the commercial parties involved in the trial?			
Is the CI a member of a committee providing advice to any of the commercial parties involved in the trial?			
Does the CI have any significant financial interests in any of the commercial parties involved in the trial?			
Are there intellectual property issues that should be highlighted?			
Does the CI or members of his/her family have any significant financial interests* in the company/manufacturer supplying the IMP/Device or funding the trial? **Significant financial interests are shares or share options, securities, payments for services such as consultancy or payments in respect of IP. IP includes license fees, royalties and revenue sharing arrangements.*			
Does the CI have any other conflict interests* in the company/manufacturer supplying the IMP/device or funding the trial? **Significant financial interests are shares or share options, securities, payments for services such as consultancy or payments in respect of IP. IP includes license fees, royalties and revenue sharing arrangements.*			
Does the CI have any other conflict interests* in the company/manufacturer supplying the IMP/device or funding the trial? **Significant financial interests are shares or share options, securities, payments for services such as consultancy or payments in respect of IP. IP includes license fees, royalties and revenue sharing arrangements.*			
Does the CI have any other conflict of interests?			

If the answer is yes to any of the questions above, please provide details:

Is the CI currently under investigation for misconduct, or for any other reason? Yes ☐ No☐

If yes above, please details:

Are there any other issues that may impede on the decision of academic institution to take on sponsorship/ EU representation for the above trial?

Yes ☐ No ☐

If yes above, please details:

Risks Identified:
Risk Level: Low ☐ Medium ☐ High ☐
Mitigation Plan:
Clinical risks The CI has enclosed appropriate written consideration to identifying, monitoring and mitigating risks associated with the sustainability of the study including; appropriate staff, training, cross-cover, governance, finances, patient consent and communication, data and GDPR oversight, sample storage, SAE and SUSAR reporting, GCP, etc. Yes ☐ No ☐ Comments: Has appropriate consideration been given to consideration of the benefit risk and are appropriate organisational structures in place to ensure appropriate response and management of same (e.g. urgent safety restrictions)? Yes ☐ No ☐
Research Ethics approval Granted ☐ Pending (the approval to proceed with the study is subject to ethics approval) ☐
Regulatory approval Not applicable ☐ Granted ☐ Pending (the approval to proceed with the study is subject to regulatory approval) ☐
Sponsor oversight role Ensure GCP compliance ☐ Carry out site initiation visit and monitoring ☐ Carry out site initiation visit only ☐ No oversight ☐
Study Risk Assessment completed by:
PI Name:

PI Signature:	**Date:**
Sponsor Representative:	
Sponsor Representative Signature:	**Date:**