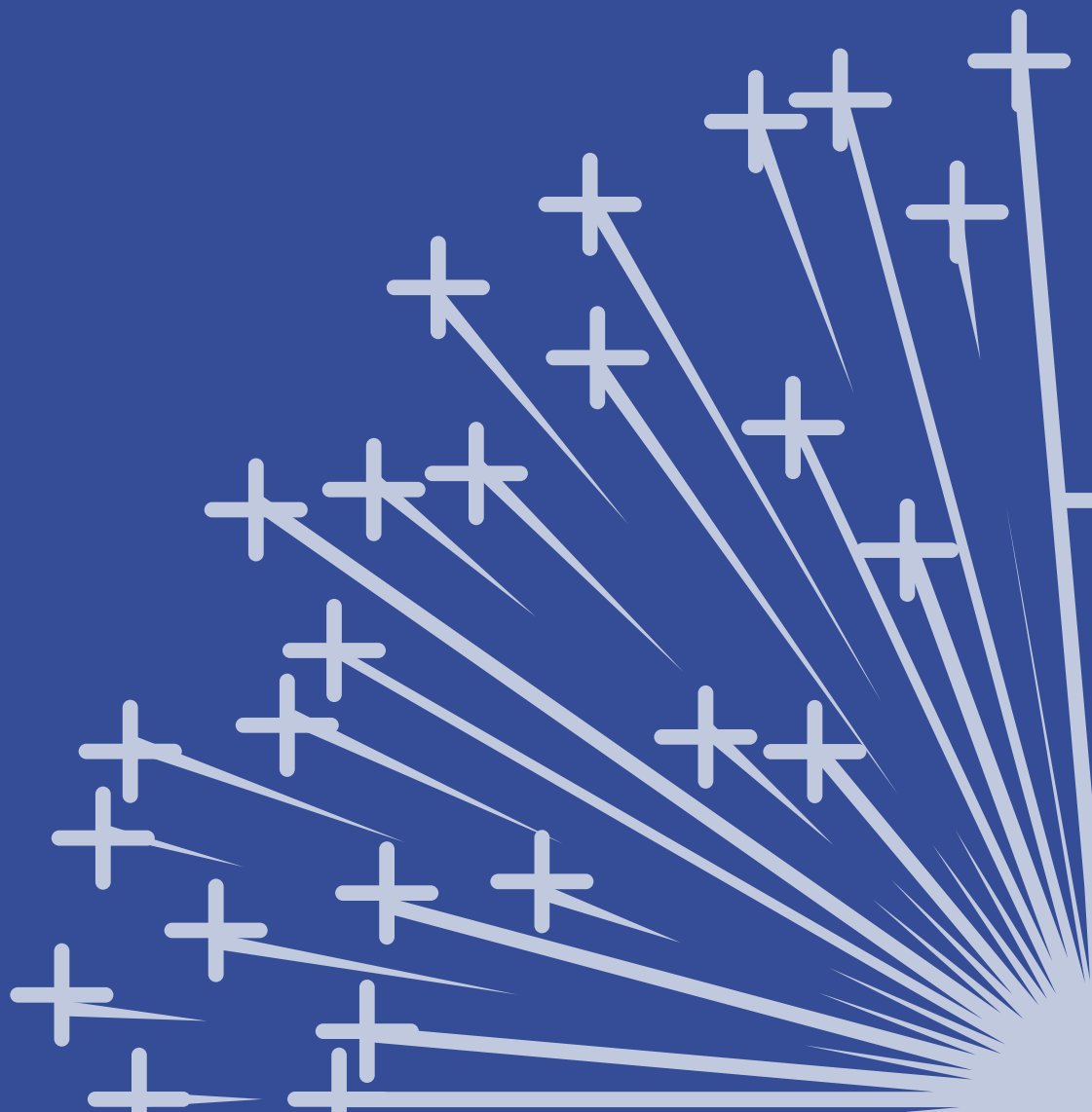


Corporate
Enabling of
Clinical Research
Report
October 2019





This report has been prepared by the Corporate Enabling of Clinical Research initiative to the best of their knowledge. While reasonable effort has been made to ensure the content and information contained in this document is accurate, neither any of the individuals nor any of the organisations who have participated in the working groups, assume any legal responsibility or liability to any user of the report nor for any errors or omissions in the report. This report is not intended to be prescriptive. This report does not constitute legal advice. Parties should take their own legal and or regulatory advice in relation to the subject matter.

Contents

Foreword	5	
Acknowledgements	6	
SECTION ONE: OVERVIEW		
1.1	Background and Purpose	8
1.2	Key Challenges	9
1.3	Corporate Enabling of Clinical Research Action Plan and Workgroup Achievements	10
1.3.1	Governance and Leadership Working Group	10
1.3.2	Sponsorship and Quality Working Group	11
1.3.3	Insurance Working Group	11
1.3.4	Contracts and Legal Working Group	12
1.3.5	Resourcing of Sponsorship Working Group	12
1.3.6	Clinician Engagement and Support Working Group	13
1.4	Additional Benefits of the CECR Initiative to Academic Institutions and Health Sector	14
1.5	Corporate Enabling of Clinical Research Contributors	15
1.6	External Contributors	16
1.7	Methodology and Management of the CECR Initiative	17
1.8	Next Steps	18
SECTION TWO: WORKING GROUPS REPORTS		
2.1	Governance and Leadership	21
2.1.1	Importance of the Collaboration Between the Academic and Health Sectors	21
2.1.2	Current Challenges	23
2.1.3	Benefits of a Cooperation Framework	23
2.1.4	Principles of Good Practice and Collaboration Agreements	25
2.2	Sponsorship and Quality	26
2.2.1	Recommendations on how to Manage Sponsorship Responsibilities	27
2.2.2	Operational Tools	28
2.3	Insurance	29
2.3.1	Achievements of the Insurance WG Activities	30
2.4	Contracts and Legal	32
2.4.1	Contractual Challenges Faced by Academic Institutions in Clinical Research Studies	32
2.4.2	Address the Contractual Challenges for Clinical Trial Networks	34
2.5	Resourcing of Sponsorship	37
2.6	Clinician Engagement and Support	39
2.6.1	Action on Clinician Engagement and Support	39
2.6.2	Key Findings and Recommendations	40

APPENDICES

Appendix I	Principles of Good Practice and Collaboration Arrangements to Deliver Clinical Studies Across the Academic and Health Sectors	43
Appendix II	Agreed Terminology	56
Appendix III	Sample Methodologies and Tools to Help Deliver Academic Sponsorship Responsibilities	62
	Annex 1: Clinical Study Registration Form	84
	Annex 2: Sponsorship Risk Assessment Form	88
	Annex 3A: Division of Responsibilities Medicinal Products	97
	Annex 3B: Division of Responsibilities Medical Devices	103
	Annex 4: Sponsor Oversight Committee Report	109
	Annex 5: Classification Based Post Approval Requirements Tables	110
Appendix IV	Contractual Framework for Data Protection	114
Appendix V	Enabling Costs	116
Appendix VI	Survey on Support for Clinicians Across the Academic Sector	117
Appendix VII	Clinical Research Support Function	123
Abbreviations		125

Foreword

Dr Paola Della Porta of Royal College of Surgeons Ireland, Ms Nora Geary of University College Cork, Prof Pat O' Mahony of Clinical Research Development Ireland - Co-Chairs of the Corporate Enabling of Clinical Research initiative.

It has been a great privilege to co-chair this initiative, focused on the *Corporate Enabling of Clinical Research in Ireland*.

Clinical Research is a vital component of any well functioning healthcare system and is also essential in the ongoing development of our academic institutions. Patient outcomes are better and academic achievement and teaching outcomes enhanced.

In addition to the clinical, scientific and technical expertise that are required for the planning and conduct of clinical research, a broad range of additional skills and expertise in the areas of insurance, sponsorship, contracts, governance, financial planning and research support are necessary to ensure that clinical research is adequately governed and managed.

As many clinical research programmes are operated across sites and institutions, it is also beneficial that, in so far as possible, practices and standards are consistent. This creates a clinical research system that is safer, agile and more efficient.

The Corporate Enabling of Clinical Research initiative built on the excellent work conducted over a number of years by colleagues from across the institutions. It brought together complementary expertise and experience of 67 colleagues and in a timely and coordinated manner it provided the impetus to address the challenges of academic institutions in sponsoring clinical research.

The work was significantly enhanced by the overall leadership and coordination provided by the project manager, Gemma Leacy, and we are grateful to Gemma for her excellent work.

Our thanks also to the institutions who sustained this initiative with their financial support.

Finally we would like to express our sincere gratitude to all who have contributed to the work described in this report which we are pleased to commend it to you the reader.

Acknowledgements

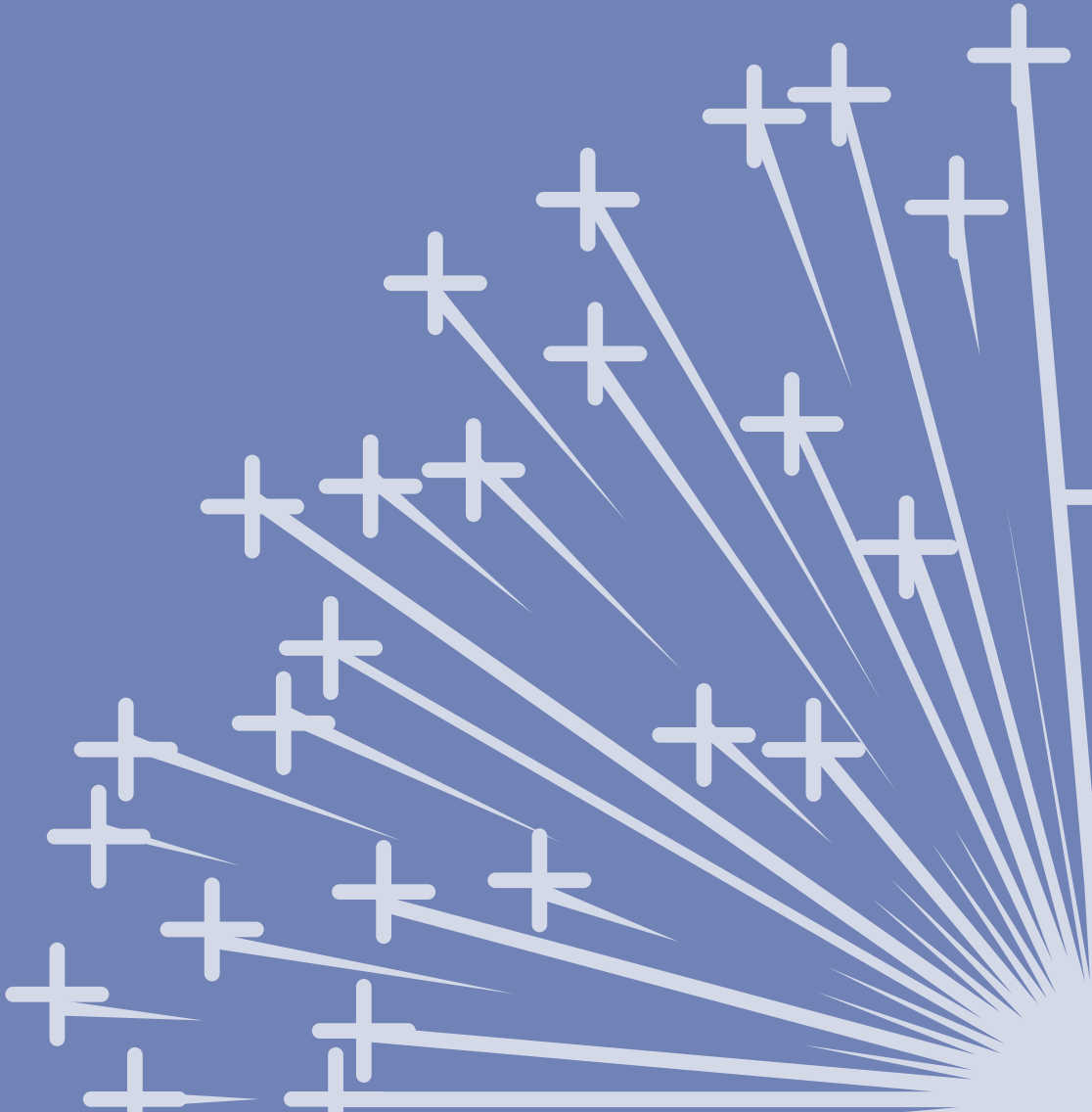
The Corporate Enabling of Clinical Research (CECR) would not have been possible without the enormous contribution and collaboration of all the stakeholders, in particular the CECR 67 working group members and partner organisations.

The partner organisations who contributed to the initiative are; National University of Ireland Galway, Trinity College Dublin, Royal College of Surgeons Ireland, University College Cork, University College Dublin, University of Limerick, Maynooth University, Clinical Research Development Ireland, Health Research Board - Clinical Research Coordination Ireland, Health Research Board, State Claims Agency, Mercy University Hospital, Beaumont Hospital, Cancer Trials Ireland, Enterprise Ireland and Health Service Executive. These organisations made a substantial in-kind contribution with the assignment of key members of staff to the planning and development of the initiative and their participation in the working group activities.

CECR project manager, Gemma Leacy, who played a fundamental role in the delivery of the project was funded by the following partner organisations; National University of Ireland Galway, Trinity College Dublin, Royal College of Surgeons Ireland, University College Cork, University College Dublin, University of Limerick, Clinical Research Development Ireland, Health Research Board - Clinical Research Coordination Ireland and Health Research Board.

Section One

Overview



1.1 Background and Purpose

Clinical research plays a key role in health research and innovation, driving the translation of research discoveries and knowledge into new ways of treating patients, delivering care, changing behaviour and ultimately improving health, wellbeing and health services. The health and economic benefits of clinical research for patients, institutions and healthcare systems are numerous and well documented. However, they require the development of a robust integrated clinical research infrastructure as well as collaboration and cooperation between academic institutions, the healthcare system and funders of clinical research.

The development of an integrated clinical research infrastructure in Ireland is a national priority¹ and many of the actions identified in the action plan for health research² in Ireland are designed to create a coherent health research system to support clinical research.

Prior to 2017, clinical research in Ireland was operated in a developing dynamic environment. A lot of progress had been made in delivering elements of clinical research infrastructure. However across the academic and health sectors there were inconsistencies of approaches and understandings on how clinical research should be governed and how sponsorship responsibilities and risks should be managed. These inconsistencies were creating inefficiencies across the clinical research system, potential risks for patient safety, and legal, financial and reputational exposure for the academic Sponsors.

In early 2017, Irish academic institutions and research funders came together under the Corporate Enabling of Clinical Research (CECR) initiative to identify and address the challenges of sponsoring clinical research studies in the areas of governance, contracts, insurance, operations, financial resources, engagement with the health sector, training and support.

¹ **National Service Plan 2018, Health Service Executive**

<https://www.hse.ie/eng/services/publications/serviceplans/national-service-plan-2018.pdf>

² **Action Plan for Health Research 2009-2013**, Department for Health

https://health.gov.ie/wp-content/uploads/2014/03/action_plan_health_research.pdf

1.2 Key Challenges

The CECR action plan was based on a gap analysis undertaken by the CECR Steering Group. The Steering Group reviewed and assessed the challenges of sponsoring and supporting clinical research, and identified the following gaps/areas for improvement:

- Engagement and cooperation between academic institutions and the health sector in relation to the planning, governance and management of clinical studies.
- Transparency and clarity on roles and responsibilities of academic institutions and hospitals in the governance and conduct of clinical studies.
- The requirement to develop a plan for assessing and managing sponsorship risk and fulfilling sponsorship responsibilities.
- The requirement for the academic sector and the health sector to develop and agree a national contractual framework for the governance and management of clinical studies.
- The requirement to achieve consistency of contractual approaches across the academic and health sectors.
- The need to agree a more timely and efficient inter-institutional approval pathway for studies and contracts which would enable smoother contracting processes and ensure that clinical studies begin within a reasonable time frame.
- The need to clarify the scope and requirements of the Clinical Indemnity Scheme (CIS) cover and clarify the gaps that need to be filled via commercial insurances.
- The need to adequately fund the resource intensive sponsorship role of academic institutions.
- The need to provide support and training for clinicians engaging in clinical studies.
- The need to recognise the importance of the role played by hospitals in clinical research and reflect it in clinical research governance and resourcing plans.

1.3 Corporate Enabling of Clinical Research Action Plan and Workgroup Achievements

To address the key challenges identified above, an action plan was developed by an overarching Steering Group and delivered by six Working Groups (WGs). Each Working Group (WG) was given a particular area to look at. The high-level objectives and outputs of the WG activities are summarised below.

1.3.1 Governance and Leadership Working Group

The Governance and Leadership WG was tasked to deliver on the following:

- Bring together all stakeholders involved in clinical research, namely the Higher Education Institutions (HEIs), funders, Health Products Regulatory Authority (HPRA), Department of Health (DoH), Health Service Executive (HSE) nationally, hospital groups regionally and constituent hospitals locally, voluntary hospitals chief executive officer forum and the State Claims Agency (SCA) to share challenges, propose solutions and seek engagement in the delivery of the action plan .
- Provide potential solutions for the contractual framework that enables (a) clinicians employed by hospitals to undertake research with academic institutions and (b) employees of academic institutions to undertake research activities in hospitals, including governance and management plans (for example in the form of memoranda of understanding/collaboration agreements and/or national protocols).
- Develop and agree with the health sector a contractual framework to govern clinical research at the planning and implementation stage; define a pathway for approval of studies; resourcing (financial and human resources); contractual matters, employment status; intellectual property (IP); setting out roles and responsibilities of all parties, oversight and contractual requirements.
- Achieve a consistent approach around terminology for clinical studies across academic institutions, in particular around classifications/types of trials.

Following an initial high-level engagement with the health sector including the SCA (who manage the Clinical Indemnity Scheme and General Indemnity Scheme), DoH, and the HSE, HPRA and funders, the CECR initiative brought together representatives from academic institutions, Health Research Board (HRB), Enterprise Ireland (EI), SCA, voluntary hospitals (Beaumont Hospital and Mercy University Hospital), Cancer Trials Ireland, and HSE.

Through engagement with the HSE, the Governance and Leadership WG were made aware that the health sector was not ready at this point to take a sectoral position on clinical research governance, resourcing and contractual matters.

Being unable to agree a contractual framework, the Governance and Leadership WG developed a document which identifies the current governance gaps, their implications and the importance and benefits of the collaboration between the academic and health sector.

The document also proposes principles of good practice, governance and management arrangements that the academic and the health sectors should jointly consider and agree in order to deliver safe and high-quality clinical studies across the academic and health sectors.

Through their participation in CECR WG meetings, representatives of the HSE have been made aware of the governance and management challenges faced by academic institutions in sponsoring clinical research and benefits that could be achieved through cooperation with the health sector.

It is anticipated that the outputs of the CECR initiative will benefit the health sector and CECR tools will be made available to them.

To address the issues around consistency of terminology, all CECR WGs developed a document which provides the agreed definitions/terminology and classifications/types of trials.

More details on the rationale and achievements of the work carried out by the Governance and Leadership WG are summarised in Section 2.1 of this document. Further details are available in Appendix I and II.

1.3.2 Sponsorship and Quality Working Group

The Sponsorship and Quality WG was tasked to:

- Define governance, management and institutional approval requirements for academic sponsorship of clinical trials and clarify the roles of academic institutions and hospitals.
- Develop a suggested inter-institutional approval pathway for the sponsorship of clinical studies.

The output of the workgroup includes recommendations, sample tools and methodologies aimed at helping academic Sponsors to deliver and manage sponsorship responsibilities.

More details on the rationale and achievements of the work carried out by the Sponsorship and Quality WG are summarised in Section 2.2 of this document. Further details are available in Appendix III.

1.3.3 Insurance Working Group

The Insurance WG was tasked with clarifying with the SCA the indemnity cover under the CIS and to achieve consistency in the procurement of commercial insurance for clinical studies across academic institutions.

As a result of the engagement with the SCA representatives in the WG activities, the SCA developed a State Indemnity Guidelines (SIG) document which clarifies the indemnities provided by CIS for national clinical trials. The SIG document also helps academic institutions ensure that their commercial insurance cover complements and does not duplicate CIS cover.

The SIG document is available on the SCA website (<https://stateclaims.ie/resources>).

The Insurance WG has provided clarity on the difference between “trial by trial” versus “whole of trials” commercial insurance policies and benefits of the latter. It also flagged the importance of consistency of terminology, contractual indemnities and clarity on roles and responsibilities from an insurance perspective. These aspects have been addressed by the other WGs.

More details on the rationale and achievements of the work carried out by the Insurance WG are summarised in Section 2.3 of this document.

1.3.4 Contracts and Legal Working Group

The Contracts and Legal WG was tasked to develop a plan for achieving consistency of contractual approaches across the sector.

The achievements of the Contract and Legal WG include:

- Identification of the contractual challenges of clinical research projects and networks, and recommendations to funders, academic institutions and the health sector to address them.
- Development of template clinical trial agreements and clinical trial network agreements, which are agreed by all Irish academic institutions and had input from the SCA. The use of these templates will achieve consistency of approaches and a greater efficiency of contractual activities across the academic and health sector.
- Development of a contractual framework for data protection.

More details on the rationale and achievements of the work carried out by the Contracts and Legal WG are summarised in Section 2.4 of this document. Further details are available in Appendix IV.

1.3.5 Resourcing of Sponsorship Working Group

The Resourcing of Sponsorship WG was tasked with developing and agreeing costing and funding models for regulated and non-regulated studies that support the engagement of hospitals in research and adequately resource academic institutions to deliver sponsorship responsibilities and to budget for clinical studies appropriately.

In the absence of an indirect cost rate that covers institutional costs for the sponsorship of clinical studies, the Resourcing of Sponsorship WG have proposed the introduction of a new cost category called Enabling Costs. The WG identified the types of sponsorship activities the enabling costs relate to and provided a number of recommendations on the additional work required to ensure that institutional enabling costs are identified and included in grant applications.

More details on the rationale and achievements of the work carried out by the Resourcing of Sponsorship WG are summarised in Section 2.5 of this document. Further details are available in Appendix V.

1.3.6 Clinician Engagement and Support Working Group

The Clinician Engagement and Support WG was tasked with identifying and addressing the challenges faced by clinicians engaging in research and the challenges of academic institutions to provide research support to clinicians.

To understand the type and level of support that academic institutions currently provide to clinicians and the degree to which the delivery of this support was coordinated within each institution, the WG carried out a survey of the support that research offices/support services (RO/RSSs) and clinical research facilities/centres (CRF/Cs) provide to clinicians across the academic sector. The WG also carried out a survey on a small group of clinicians to understand their perspective of the support available to them and gaps that needed to be addressed.

The WG made a number of recommendations for the provision/delivery of support in the areas of project management, pre- and post- award activities, administration, ethics, and the coordination/liaison of research support services with clinical research support activities. The WG also recommended consideration of the provision of protected research time for clinicians (at all levels) for research and for the development of career pathways incorporating research.

More details on the rationale and achievements of the work carried out by the Clinician Engagement and Support WG are summarised in Section 2.6 of this document. Further details are available in Appendix VI and VII.

1.4 Additional Benefits of the CECR Initiative to Academic Institutions and the Health Sector

Figure 1: Benefits of the CECR Initiative



The CECR initiative delivered benefits which went beyond the ambition of the action plan. It enabled a dialogue with academic institutions, funders, SCA, hospitals and HSE on the institutional challenges of clinical studies and brought together the perspective of key stakeholders in the delivery of the CECR action plan. This engagement highlighted the importance of cooperation between academic institutions, funders and the health sector to deliver a sustainable and safe clinical research system.

It leveraged a critical mass of professionals with substantial and complementary experience and expertise in senior management, clinical research regulations, legal, public funding, risk management, clinical research support, finance, research management and research support services.

It demonstrated the complexity associated with the sponsorship of clinical trials and the absolute requirement for a whole sector and inter-sectoral cooperation to deliver a safe and efficient clinical research system for the safety and benefit of patients.

The cooperative work undertaken under CECR improved the working relationship between

academic institutions at various levels and in different areas of the organisations involved and demonstrated the importance of cooperation to achieve consistency of approaches, improve practices, and deliver better coordinated and more timely inter-institutional activities.

CECR funding of €135k (contributed by member institutions) to deliver the action plan proved great value for money. In addition to supporting the project manager, the funding was also used for the procurement of external advice/expertise in the areas of clinical research contracts, commercial insurance, data protection and clinical research regulation. External legal and regulatory advisors also contributed to training and the development of resources which is helping institutions to deliver sponsorship responsibilities in a consistent manner and in creating a more coherent and efficient clinical research system.

The training and engagement with institutions and consultants who had significant experience and expertise in the sponsorship of clinical trials and upskilled members with limited or no experience at the start of this initiative.

1.5 CECR Contributors

The CECR initiative was hosted by Clinical Research Development Ireland (CRDI) which is a not-for-profit research partnership comprising of the National University of Ireland Galway (NUIG), Royal College of Surgeons in Ireland (RCSI), Trinity College Dublin (TCD), University College Cork (UCC), University College Dublin (UCD) and University of Limerick (UL).

CECR founding members included NUIG, TCD, RCSI, UCC, UCD, UL, HRB, CRDI and Health Research Board Clinical Research Coordination Ireland (HRB CRCI). Representatives from Maynooth University, EI, Cancer Trials Ireland, Mercy University and Beaumont Hospitals, SCA and HSE joined at a later date. The importance of the HSE's involvement in the initiative was recognised. A number of engagements took place with senior personnel in the HSE to seek nominations. In November 2017, a HSE corporate representative joined the Governance and Leadership WG, with further representatives joining a number of WG in June 2018. The HSE opted to join the CECR WGs in an observer capacity.

The initiative, including the Steering and the Governance and Leadership WG, was co-chaired by Dr Paola Della Porta of RCSI, Nora Geary of UCC and Prof Pat O' Mahony of CRDI. Gemma Leacy was employed as CECR project manager.

Overall 67 people participated in the development and implementation of the CECR action plan. They contributed to one or more WG activities and brought expertise ranging from financial, to quality and regulatory affairs, risk management, governance and legal affairs, research support and senior management to individual WGs.

1.6 External Contributors

The **State Claims Agency** support of the CECR initiative is greatly appreciated. Ciaràn Breen, Director SCA, has been fundamental in the development of clinical research infrastructure in Ireland. Pat Kirwan, Deputy Director and Fiona Kearns, Senior Enterprise Risk Manager, participated in the Insurance WG and put a lot of time and effort into preparing the SIG document. They also engaged with the Contracts and Legal WG in providing input into the clinical trial agreements.

Willis Towers Watson: Tina O Keeffe, Head of Cork and Client Services and Susan Cavanagh, Account Executive were members of the Insurance WG and provided expert insurance advice to the group while working closely with the SCA in assisting in preparing the SIG document.

Imperial College London: Dr Paul Craven, Head of Research Operations at the National Institute for Health Research Imperial Biomedical Research Centre, hosted a very extensive and useful meeting between representatives of CECR WGs and staff of the Imperial Clinical Trial Unit, the Imperial National Health Service (NHS) Trust Joint Research Office (including legal team), the Joint Research Compliance Office and one of the NHS Trust Research Facilities. At the meeting, CECR representatives had the opportunity to learn how the Imperial NHS Trust delivers oversight, manages sponsorship responsibilities and provides support for clinical trials activities. The learnings from this meeting have been beneficial for all the CECR WG activities.

Neasa Greene Consulting Ltd was engaged on a consultancy basis to provide training and advice on sponsorship responsibilities and quality and regulatory aspects of clinical investigation of medical devices.

Paul Cross Consulting Ltd was engaged on a consultancy basis to provide regulatory advice on the sponsorship document.

The legal firm **Ronan Daly Jermyn** was engaged for the provision of legal expertise in clinical studies and data protection. They contributed to the development of template network agreement and clinical trial agreements.

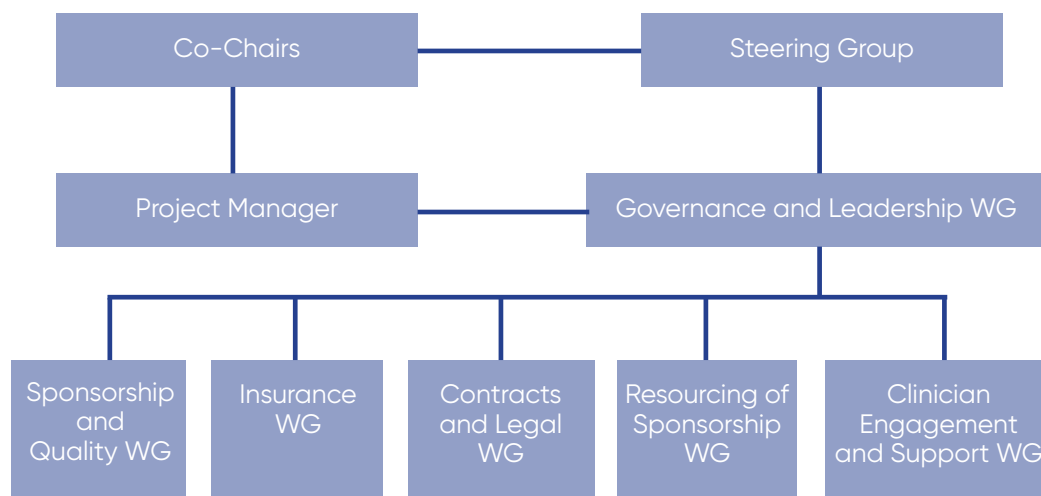
European Centre for Clinical Research Training provided training in legal aspect and risk management of clinical studies.

1.7 Methodology and Management of the CECR Initiative

The action plan was delivered in the time frame of one year (2018) using a project management approach.

The CECR management structure (outlined in the organigram below - Figure 2) included a Steering Group and six WGs namely; Governance and Leadership, Sponsorship and Quality, Insurance, Contracts and Legal, Resourcing of Sponsorship and Clinician Engagement and Support.

Figure 2: CECR Management Structure

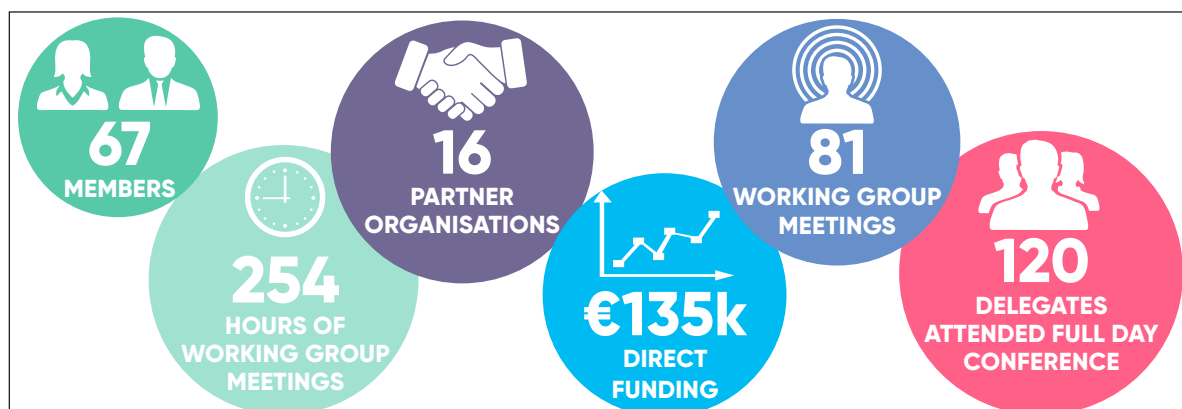


Each **WG** was responsible for the delivery of one of the high-level objectives of the action plan. Each **WG** developed a Work Plan with key deliverables. Co-chairs and members are listed at the start of each **WG** report in Section 2.

The **Governance and Leadership WG** included all **WGs** co-chairs and senior management representatives from the organisations involved in the initiative. The **WGs** role was to monitor and support all **WG** activities and provide feedback on the **WG** reports.

The **Steering Group** was inclusive of all contributors to the initiative and met on a quarterly basis to review the progress of the action plan.

Figure 3: CECR in Numbers



1.8 Next Steps

While significant progress has been made by this initiative, further key steps are required to ensure that the initiatives realises the full benefits. These include;

1. Continue the engagement with the health sector to
 - Put in place a contractual framework between each academic institution and its affiliated Hospital Group, which governs clinical research. Alternatively establish a legal relationship via legislation.
 - Agree the terms and conditions of honorary/adjunct affiliations of clinicians with academic institutions for the conduct of clinical research.
 - Agree the arrangements/approval requirements to enable academic employees to support clinicians in the hospitals for the conduct of clinical research.
 - Identify the costs sustained by hospitals to host and support clinical research activities. Explore models for quantifying and budgeting such activities.
 - Develop career pathways which support clinician engagement in research, including protected time for research and career progression models.
 - Identify and address the health sector requirements/needs in grant applications.
 - Explore/agree approval requirements, terms and a contractual framework for setting up networks, with the view that health organisations involved in clinical trial networks become signatories in network agreements
2. Adopt the template agreements developed by the Contract and Legal WG and obtain buy-in from the health sector.
3. Continue the engagement with the HRB and possibly other funding bodies on contractual matters and hold meetings with them when new contractual issues arise.
4. Engage with funders to agree realistic timelines for contract drafting and negotiation so that funders take them into account when setting project/programme start and end dates.
5. Engage with funders to ensure that all institutions involved in a collaborative clinical research project/programme have the opportunity to review and approve the project/programme at grant application stage .
6. Engage with the SCA and the DoH to ensure that the Government approves the Delegation Order proposed by the SCA to include institutions CRF/Cs as Delegated State Authorities (DSAs).

Delegated State Authority (DSA) - refers to all bodies delegated to the SCA, it includes the HSE hospitals and community healthcare organisations (including section 38 voluntary hospitals and disability sector) and some section 39s delegated to the CIS only.

7. Continue the engagement and cooperation among academic institutions to address any future contractual matters in a timely manner.
8. Ensure that the research overhead rate review, which involves funding agencies, government departments and the Irish Universities Association, include clinical research and a full economic costing model for clinical research is developed.
9. Engage further with the Royal College of Physicians Ireland to explore the possibility of including clinical research in the formal training programmes for clinicians.
10. Disseminate the CECR report as widely as possible so that the resources/tools developed by CECR WGs are used and adapted, as appropriate.

Section Two

Working Group Reports



2.1 GOVERNANCE AND LEADERSHIP

Co-Chairs of the WG: *Dr Paola Della Porta (RCSI), Nora Geary (UCC), Prof Pat O Mahony (CRDI)*

Contributors: *Dr Seamus Browne (RCSI), Bernadette Costello (NUIG), Pauline Cronin (NUIG), Michèle Cunnane (HRB CRCI), Sandra Daly (MUH), Dr Noel Daly (EI), Cliona Donnellan (UL), Prof Peter Doran (UCD), John Gaffney (NUIG), Dr Aoife Gallagher (RCSI), Dr Orla Healy (HSE South), Prof Martina Hennessy (TCD), Audrey Huggard (UCC), Dr Fionnuala Keane (HRB CRCI), Dr Fiona Manning (RCSI), Anne McNealy (Beaumont Hospital), Eibhlin Mulroe (Cancer Trials Ireland), Barry O'Brien (UCC), Dr David O'Connell (UCC), Aengus Parson (NUIG), Mary Tracey (TCD), Dr Claire Walsh (EI), Oonagh Ward (HRB)*

Observers: *Dr Natalie Cole (HSE), Sarah Dever (HSE), Dr Ana Têrres (HSE)*

2.1.1 Importance of the Collaboration Between the Academic and Health Sectors

Clinical research is essential to deliver better health and care, which in turn can improve the quality of life. To achieve this, clinical research should be ethical, scientifically sound, and put the safety and well-being of the individual before the interests of science and society.

The development of a robust integrated clinical research infrastructure in Ireland is a national priority and requires engagement and collaboration between academic institutions, the healthcare system and funders of clinical research.

The academic and health sectors play complementary and essential roles in the conduct of clinical research by providing infrastructure, by jointly contributing to the provision of resources, by providing expertise and support and sharing benefits, costs and risks.

Their collaboration is beneficial because:

- It promotes interactions between scientists and clinical researchers with no academic affiliation thus fostering cross-fertilisation between basic scientific concepts and clinical needs; this in turn can lead to the development of new therapeutic approaches and diagnostics, improved health outcomes for patients and service delivery.
- It provides clinicians with greater opportunities and support for innovation, including engagement with industry and commercialisation.
- It provides clinicians with training and development opportunities that are required for career advancement, which, in turn, facilitates the attraction and retention of talented clinicians and research staff and provides overall for improved healthcare delivery.

Further and enhanced collaboration between the academic sector and health sector would also support the engagement that is required to address the legal, operational, governance,

insurance/indemnity challenges that both sectors currently face to deliver clinical research which is discussed later in this report. Clinical research is very resource intensive and comes with substantial costs, which are shared by both sectors and should therefore be assessed and managed jointly.

Moreover, if clinical research is not adequately planned, supported, managed and governed and risks are not adequately considered and addressed across both sectors, the safety of patients can be put at risk and potentially lead to financial and reputational damage for both the hospital and the academic institution.

To avoid this, it is necessary that the health and academic sectors engage further, agree on the principles of good clinical research practice and put in place a collaboration framework, which sets the terms and scope of their collaboration.

Given the importance of the role played by the health sector in clinical research, its engagement and collaboration with the academic sector are fundamental for the successful implementation of the CECR plan to deliver a safe and functional clinical research system in Ireland.

This section of the report identifies the governance, legal, and insurance challenges of enabling academic clinical research and proposes principles of good practice, governance and management arrangements that the academic and the health sectors could jointly implement in order to deliver safe and high-quality clinical research across the academic and health sectors.

The proposed principles and arrangements could be applied to any research activities, regardless of the funding source and sponsor identity, whereby:

- The academic institution and the affiliated hospital share personnel, equipment, facilities, information or other resources

and where

- The chief investigator (CI) who is responsible for conducting the research activities is either jointly employed by a hospital and an academic institution or is a hospital employee with an academic affiliation.

Or

- Staff involved in the research are academic institution employees working in a hospital under the supervision of a hospital employee.

The principles are not intended to override any existing governance structure or policy/code of conduct in place at individual institutions.

Their adoption should therefore take into consideration each specific institutional and collaborative context.

2.1.2 Current Challenges

Requirements to develop and agree a Joint Governance and Management Plan for clinical research.

Irish hospitals and academic institutions play interdependent roles in clinical research but there is not an agreed overarching governance and management framework in place.

To address this gap, academic sponsors put in place a clinical trial agreement (CTA) which sets out the governance arrangement for each clinical trial on a case by case basis.

In the absence of ongoing consultation between the sectors, when contracting with funders, academic institutions are required to make commitments to deliver on clinical research activities over which they may not have full control.

Necessity to develop a contractual framework, which sets the terms of HSE consultants' engagement with academic institutions in research and institutional employees' access to hospital's patients, facilities and resources.

At present there is no contractual framework that sets the terms and conditions of the engagement of HSE/voluntary hospital consultants with academic institutions in research. Likewise, there are no agreed terms and conditions for the placements of academic employees in hospitals and/or access to hospital patients, facilities and resources. This creates regulatory, legal and insurance gaps for academic institutions, hospitals and CIs and a potential exposure for all parties involved, including patients.

In the case where CIs have a joint affiliation to a hospital and an academic institution, it is not always clear whether they are acting in their clinical or academic capacity, and therefore where the institutional responsibility and liability rests.

Clarity on terms of affiliation (between employment or adjunct), activities, institutional responsibilities and ongoing engagement with the State Claims Agency (SCA) would help identify and address any insurance/indemnity gaps.

The lack of clarity on terms of affiliation in the area of ownership and management of intellectual property (IP) also makes it difficult for academic institutions to contract with funders and other institutions/third parties if IP is an important part of the output of the clinical study.

2.1.3 Benefits of a Cooperation Framework

An overarching collaboration framework between the academic and health sectors would help ensure that clinical research is planned and delivered in a coordinated, informed, effective and concise manner, according to international best practice, in compliance with funders' terms and conditions and applicable regulatory requirements and guidelines. Most importantly, it would help safeguard patient safety, wellbeing and rights to privacy.

To be helpful, the framework should identify the areas of cooperation, approaches and expectations, roles and responsibilities, benefits, terms and conditions.

In particular, it should clarify:

- The role of hospitals in the governance of clinical studies sponsored by academic institutions and others like Cancer Trials Ireland.
- The terms and conditions of clinician engagement with academic institutions for the conduct of research.
- The terms and conditions of academic employees' placements in hospitals and/or their access to hospitals' patients, facilities and resources.
- Data protection arrangements.
- Institutional approval pathways and requirements for study plans, acceptance of funding awards and sponsorship of clinical trials.
- The contractual approach to clinical trials and collaborative clinical research programmes.
- The approach to financial planning and allocations of funding between the academic and the health sector.
- The approach to indemnity/insurance cover.
- The approach to ownership and management of IP generated by investigators who are hospital employees and have an affiliation with an academic institution.
- Principles and measures required to enable good clinical practice, research integrity and health and safety in research.

This document does not prescribe the content of a contractual framework but rather proposes general principles and cooperation arrangements that may help address the challenges described above.

Any principle, governance and management arrangement proposed in this document is not intended to override any existing governance structure or policy/code of conduct in place at individual institutions. Their adoption should therefore take into consideration each specific institutional context.

2.1.4 Principles of Good Practice and Collaboration Arrangements

The management arrangements and the principles of cooperation proposed by the CECR Governance and Leadership WG (which are available in Appendix I of this document) are aimed to achieve clarity and as much as possible consistency on the following:

- The terms of engagement of employees of one sector in research activity involving resources of the other.
- The role and responsibilities of CIs and students engaging in clinical research.
- The role, responsibilities and requirements for academic sponsored clinical trials.
- Clinical research governance, including approval, requirements and arrangements.
- Ownership and management of IP.
- Approach to costing of research, distribution and transfer of funding.
- Approach to liability, insurance and indemnities.
- Approach to contracts, including partner engagement and approval.
- Investigators' compliance with (a) institutional policies and procedures, (b) code of conduct for clinical research and (c) National policy statement on ensuring research integrity in Ireland.
- Competence, quality and integrity requirements.
- The role of the clinical research facilities/centres (CRF/Cs) and clinical research support requirements with regard to financial support, training, mentoring, supervision and access to hospital patients, facilities, and data.
- Dissemination.
- Patient engagement.
- Access to patients, patient material and information.
- Collection, use and storage of human tissue, fluids and organs.
- Health and safety.

2.2 SPONSORSHIP AND QUALITY

Co-Chairs of the WG: *Dr Paola Della Porta (RCSI), Dr Fionnuala Keane (HRB CRCI)*

Contributors: *Dr Elaine Breslin (NUIG), Dr Caitriona Creely (HRB), Dr Muiris Dowling (UCC), Rabia Hussain (UCD), Dr Margaret Lawlor (UL), Dr Fiona Manning (RCSI), Hannah McCarthy (TCD – Cancer Trials Ireland), Brenda Molloy (UCD), Dr Ellen Moran (HRB), Carole Schilling (RCSI), Fergal Seeballuck (TCD), Dr Kathleen Scott (Cancer Trials Ireland), Oonagh Ward (HRB)*

Observers: *Dr Natalie Cole (HSE), Sarah Dever (HSE)*

Multi-institutional academic sponsored clinical studies are becoming more commonplace in Ireland and clinical research support infrastructure is now in place and continuously evolving to facilitate its delivery. However, sponsorship of clinical trials is a significant undertaking for academic institutions. It requires compliance with regulatory requirements; governance, pharmacovigilance, coordination of institutional functions responsible for regulatory compliance, pre and post-award research support, risk assessment and management, insurance/indemnity, contracts, clinical research management and support and sustainability planning. Sponsorship decisions can be very complex, onerous and, if they are not well informed, could have major institutional implications.

It is therefore important that sponsorship risks are adequately assessed, and sponsorship decisions are carefully considered. Coordination is also required among different institutional functions (research support services, legal/contracts, insurance/indemnity, finance, regulatory and clinical research support) to assess, plan and support requests for sponsorship of clinical studies throughout the study lifecycle. A high degree of clarity on institutional procedures, coordination and timelines of activities are required from the moment a study is conceived, during the preparation of funding proposals, the submission and assessment of request for institutional sponsorship, the submission of applications for regulatory and ethical approval, the drafting and negotiation of contracts, the preparatory work for the initiation of the study, the assessment of the clinical site readiness prior to commencement of the clinical trial and ongoing oversight during the lifecycle of the study.

A governance structure and a management plan are necessary to ensure that sponsorship decisions are transparent, well informed, sustainable, aligned with institutional strategies, and that adequate oversight mechanisms are in place to fulfil the sponsorship responsibilities and address any issues that may arise. The level of oversight required during the implementation of the study should be assessed carefully and be commensurate with the study's risk level.

The Sponsorship and Quality WG was tasked to identify and propose recommendations to address the challenges faced by Irish academic institutions to deliver sponsorship responsibilities for clinical trials led by affiliated clinicians.

The output of the work undertaken by the Sponsorship and Quality WG builds on the experiences of different Irish academic institutions and takes learnings from international systems.

It includes recommendations, samples tools and methodologies aimed at helping academic Sponsors to deliver and manage sponsorship responsibilities.

2.2.1 Recommendations on how to Manage Sponsorship Responsibilities

- Ensure that any clinical study carried out by academic institution's employees or affiliates such as adjunct/honorary, involving patients, patient data or material and requiring institutional support and sponsorship (where applicable), are registered and reviewed.
- Ensure that clinical studies are risk classified so that sponsorship decisions are informed, and oversight and insurance/indemnity cover are in place, as appropriate.
- Ensure that clear clinical studies' registration and review procedures are in place.
- Consider sponsorship risks and mitigation plans to inform sponsorship decisions.
- Have a clear and well-communicated sponsorship governance plan that ensures that sponsorship oversight is delivered throughout the lifecycle of the study and sponsorship decisions are well informed and in compliance with good clinical practice (GCP).
- Ensure that sponsorship decisions are documented and justified.
- Ensure that approval and oversight requirements, support activities and contracts are delivered in a coordinated and timely manner (see Contracts and Legal Section 2.4 and Clinician Engagement and Support Section 2.6).
- Ensure clarity around the role and responsibilities of the individuals and groups that help deliver these processes.
- Ensure that guidance documents and training (as necessary) are in place to assist all stakeholders (See Section Clinician Engagement and Support Section 2.6).
- Ensure the resource for the planning and implementation of the clinical study are proportionally costed in research grant proposals (see Resourcing of Sponsorship Section 2.5).
- Ensure that there is a detailed clinical trial agreement (CTA) (where applicable) in place between the Sponsor and the site(s) and that all roles, responsibilities and expected deliverables are clearly defined and agreed (see Contracts and Legal Section 2.4).

2.2.2 Operational Tools

To address the recommendations above, the Sponsorship and Quality WG developed a number of tools/documents which are available in Appendix III of this report, including:

- An example of a governance and management model for academic Sponsors, including suggested roles and responsibilities of the individuals and groups involved.
- A clinical trial classification-based methodology (including template forms and flowcharts) for streamlining sponsorship risk assessment and determining approval, planning and oversight requirements, it is recognised that for (HPRA) regulated studies further risk assessment should be carried out as per ICH GCP E6 R2³.
- A methodology and tools that could be used to identify, document and manage institutional risks so that sponsorship decisions are well informed and transparent.
- Examples of approval and planning pathways that can help ensure coordination and timeliness of institutional activities (study planning, budget review, sponsorship approval, endorsement of funding application, confirmation of insurance/indemnity, regulatory and ethical approval, contracting).
- A suite of template documents (clinical study registration form, sponsorship risk assessment form, division of responsibilities tables, sponsor oversight committee report) that can help classify studies in terms of risks, determine sponsorship requirements, document risk assessments and mitigation plan and document sponsorship decisions (Annex 1 – 5).
- Tables of standard sponsorship requirements depending on where the study fits in the clinical trial classification.

These operational tools are intended to help institutions manage their sponsorship role. They are piloted on a small number of clinical trials; they will evolve and be adjusted as learning occurs. Their use should also take into account the pre-existing local organisational, management, support arrangements and the availability of resources.

³ **Guidelines for Good Clinical Practice 2016, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use**

https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2_Step_4_2016_1109.pdf

2.3 INSURANCE

Co-Chairs of the WG: Cliona Donnellan (UL), Pauline Cronin (NUIG – from July 2018), Bernadette Costello (NUIG – until July 2018)

Contributors: Fiona Kearns (SCA), Dr Peter Coulahan (UCD), Michelle Kelly (RCSI), Pat Kirwan (SCA), Dr Margaret Lawlor (UL), Pat O Donnell (TCD), Kathryn O Driscoll (UCC)

Observers: Dr Natalie Cole (HSE), Sarah Dever (HSE/CRDI/HRB CRCI)

The issue of insurance and indemnity is one of the issues at the forefront of all commitments to clinical studies, both locally (with affiliated hospitals) and with multi-site institutional partners.

Hospitals and academic institutions play essential and complimentary roles in clinical studies. It is therefore important that insurance and indemnities are in place to cover both parties. It is essential that gaps or duplication of insurance cover are identified and managed.

The CECR initiative was set up to achieve three objectives in the area of insurance/indemnity:

- To clarify the level of indemnity provided by the State Claims Agency (SCA) and establish where cover needs to be provided by commercial insurers to dovetail with that provided by the Clinical Indemnity Scheme (CIS) and the General Indemnity Scheme (GIS).
- To achieve a consistent approach and understanding across academic institutions on procurement of commercial insurance for clinical research.
- To propose principles of good practice in the area of insurance of clinical research in Ireland.

To deliver on these objectives, as a first step, the Insurance WG undertook a review of the approach to insurance cover and indemnities for clinical research across the academic sector.

A questionnaire was developed and circulated to academic institutions, which looked at the following aspects of insurance:

- The type of insurance policies held relevant to clinical research.
- The levels of indemnity/liability provided within these insurance policies.
- The relevant exclusions noted on the policies.
- The institutions' understanding of what indemnity was provided to them by the SCA CIS.

The key findings of the review were as follows:

- There was a lack of understanding of the CIS indemnity provided by the SCA CIS, which in turn lead to a lack of consistency of approach to commercial insurance.

In general, the review showed that academic institutions were not clear to what extent the CIS would cover patient focused research sponsored by academic institutions and what additional commercial insurance cover was therefore required.

- There was a lack of clarity on the insurance requirements to enable academic employees engage in clinical research activities based in hospitals.
- Depending on the type of clinical trial/study, there was a lack of a consistent approach to indemnity.
- The contributing factors to the lack of a consistent approach to indemnity included:
 - lack of consistency around terminology.
 - lack of clarity on roles and responsibilities of the parties involved in academic sponsored clinical studies, which in turn inform indemnity and insurance arrangements.
- There was a lack of clarity on the SCA CIS indemnity position in respect of clinical trials, protocol liability, product liability and no-fault compensation.
- There was a lack of understanding by some academic institutions of the types of commercial clinical trials policies such as “trial by trial” basis or a “whole of trials” cover.

Some institutions did not know that it was possible to procure/negotiate ‘whole of trials’ insurance policies and had insurance cover on a trial by trial basis. In the latter type of arrangement, cover and fees are assessed by the insurer on a case by case basis. This arrangement did not enable academic institutions to negotiate insurance fees and anticipate insurance costs at the beginning of the insurance policy year.

To deliver on the objectives and address the issues outlined above, colleagues from the SCA were invited to join the Insurance WG.

2.3.1 Achievements of the Insurance WG activities

Clarity on the level of indemnity provided by the SCA and cover to be sought from commercial insurers

The active engagement of the SCA with the Insurance WG helped clarify the indemnity under the CIS and the cover academic institutions need to purchase via the commercial insurance market.

In collaboration with the CECR WG members, the SCA developed the SIG document. The SIG document (which is available on the SCA website - <https://stateclaims.ie/resources>) clarifies the scope of the indemnities under the CIS, the conditions/requirements associated with the indemnity and the types of cover academic institutions should consider placing with commercial insurers.

Clarification about how the indemnity schemes operated by the SCA and commercial insurance should operate together to ensure all liabilities including employers' liability, clinical trials liability, public liability, professional indemnity, products liability are covered and in instances where the research is conducted in private hospitals or by "private" clinicians such as or general practitioners or private consultants and where research is conducted in private hospitals.

Consistent approach and understanding on procurement of commercial insurance

Academic institutions who were purchasing insurance cover on a "trial by trial" basis became aware of the possibility to procure a 'whole of trials' insurance policy. This type of cover requires that each year the insured institution issues a pipeline (or schedule) of clinical trials that are expected to be carried out over the following 12 months. This information provides clinical trial insurance underwriters with a 12-month view of activity which enables them to provide best value for money and breadth of clinical trial insurance cover for the requesting institution.

Consistency Around Indemnity

To achieve consistency of approach around indemnity, the Insurance WG engaged with the Contracts and Legal WG to ensure that they would include standard indemnity clauses reviewed and agreed by the SCA in the template agreements for academic sponsored clinical trial. This standard clause has been included in the clinical trial agreement (CTA) (refer to www.crdi.ie/corporate-enabling-of-clinical-research-for-templates).

Clarity on the Responsibilities of the Parties Involved in Clinical Studies

To ensure clarity around responsibilities, the Insurance WG engaged with Sponsorship and Quality WG to develop a sample division of responsibilities table (Annex 3A and 3B) which enables the sponsor to allocate and document the responsibilities of all parties involved at all stage of a clinical trial. The roles and responsibilities framework have been included by the Contracts and Legal WG in the template CTA.

2.4 CONTRACTS AND LEGAL

Co-Chairs of the WG: Audrey Huggard (UCC), Mary Tracey (TCD)

Contributors: Cillian Bergin (UCD), Caroline Brennan (UCD), Emer Cunningham (UCD), Dr Paola Della Porta (RCSI), Sarah Dever (TCD-CRDI/HRB CRCI), Hazel Flynn (UCD), Michelle Kelly (RCSI), Ian Knight (NUIG), Paddy Martin (UCC), Miriam Ryan (MU), Dr Aoife Shannon (Cancer Trials Ireland), Oonagh Ward (HRB)

Observers: Dr Natalie Cole (HSE), Sarah Dever (HSE)

One of the main drivers of the CECR initiative has been the need to solve the inconsistency of contractual approaches for clinical research across the sector.

The Contracts and Legal WG was tasked to review the contractual challenges faced by academic institutions in clinical research studies and networks and develop and implement a plan for addressing them.

2.4.1 Address Contractual Challenges Faced by Academic Institutions in Clinical Research Studies

2.4.1.1 Achieve Consistency of Contractual Approaches and Ensure a Timely use of Project Resources

Contractual activities for clinical studies can be very time consuming and resource intensive, especially if institutions adopt different contractual approaches/architectures and template agreements. Inconsistency of contractual approaches and funding agreement with unrealistic project start dates (not taking into account the time required to put in place agreements) have a negative impact on the availability of project resources. It often occurs that as soon as the project/programme is due to start (as set by the funding agreement), investigators commit project funding for the recruitment of central resources (such as research nurses/coordinators/project managers). These resources, however, are unable to fulfil their roles in full until legal agreements are in place. This leads to a shortfall of resources towards the end of the project/programme and contractual and financial exposure for the lead institution.

Recommendations for Achieving Consistency of Contractual Approaches:

- Academic institutions, funders and health sector should consider and agree a common contractual architecture.
- The academic and the health sectors should adopt the CECR network and clinical trial agreement (CTA) templates available (refer to www.crdi.ie/corporate-enabling-of-clinical-research-for-templates) and the data protection contractual framework described in Appendix IV of this report.

The templates agreements (adapted for investigational medicinal products (IMPs), devices and non-regulated investigational studies), include data protection clauses which meet the

requirements of Article 28 of General Data Protection Regulation (GDPR)⁴. The new templates can also be used where a second academic institution is involved in a trial or is providing financial management and/or trial support.

It is anticipated that the adoption of these template agreements will benefit the clinical research system in Ireland. Templates have been very beneficial for clinical research and innovation activities in Ireland. For example the European Simplified Consortium Agreement (DESCA) template has been helpful for collaborative projects in Europe and Knowledge Transfer Ireland (KTI) for template for collaborative projects in Ireland.

Recommendations to Ensure a Timely use of Project Resources:

- Academic institutions and funders should agree realistic timelines for contract drafting and negotiation so that funders take them into account when setting project/ programme start and end dates.

Funders should also consider one of the following approaches for project start dates and contracts;

- Introduce a condition that the execution of collaboration agreements is required prior to any commitment of funding.
- Introduce a “condition precedent” in funding agreements which give institutions a certain defined period to conclude agreement from the funding award date/in advance of the project commencement.
- Introduce a phased approach whereby limited funding can be committed and spent for organisational activities leading up to sign off of the collaboration agreement (parallels could be drawn from HRB ethical approval).

2.4.1.2 Ensure Timely Review/Approvals of Collaborative Projects at Contract Negotiation Stage

Funders in Ireland generally require the endorsement of collaborative grant applications and the acceptance of collaborative funding awards by the lead institution only.

Partner institutions (such as partner academic institutions, hospitals and other sites) are therefore not necessarily given the opportunity to review and approve aspects of the proposal (for example budget, affiliation of the chief investigator (CI) , clinical trial plan and risks, role of the clinical research facility/centre (CRF/C), governance plan) which are fundamental to assess their ability to fulfil their role in the collaborative programme. This assessment is only made when partner institutions are asked to review the collaboration agreement. At that point research, management and resources plans are already set, given the challenges in engaging with hospitals, there is no time to seek hospitals commitment in the participation in the programme, budget allocations cannot be easily amended, changes in the governance/

⁴ **Data Processing Commission 2018, Guidance: A Practical Guide to Data Controller to Data Processor Contracts** <https://www.dataprotection.ie/en/organisations/guidance-practical-guide-data-controller-data-processor-contracts>

management plan can be difficult and very time consuming and issues around affiliation may be difficult/impossible to solve. Moreover, institutional sponsorship risk assessments may even conclude that the institutional risks are too high for the funded clinical studies to go ahead.

As a result of the above, contract negotiations can be very lengthy and academic institutions can be left with a budgetary shortfall and, in the absence of hospitals' approval, can be required to make a contractual commitment to deliver on clinical study activities over which they have limited/no control.

Recommendations:

- At grant application stage, funders seek commitment of all partners (academic and hospital sector as the case may be, in which the role and the budget of each institution is defined/clear).

This can be achieved in two possible ways:

- (a) All parties sign the grant application in which the role they are assuming is clear.
- (b) *The lead institution provides confirmation to the funder that it has attained institutional sign off, based on a template letter provided by the funding agency.

*HRB and academic institution preferred option.

- The academic sector clarifies with the health sector whether hospitals should review and approve grant applications, or if it would be satisfactory that this responsibility is formally delegated to the affiliated academic institution. The possibility should also exist that another institution can join the collaboration at a later date by way of accession to the collaboration agreement or otherwise.

- Funders ensure that governance and management plans include roles and responsibilities, are evaluated carefully as part of the review process and a dedicated application review criterion is put in place.

2.4.1.3 Achieve Consistency of Terminology Across the Clinical Research System

Consistency and clarity of terminology is very important from a contractual perspective. The Contracts and Legal WG therefore adopted the terminology agreed by the CECR WGs in the template agreements.

2.4.2 Address the Contractual Challenges for Clinical Trial Networks

Background

Clinical trials network (CTN) are collaborative research initiatives which bring together CIs, health professionals, health researchers and clinical research staff from different academic and health care institutions to conduct multi-centre clinical trials in a particular disease or

health area. In Ireland some of the CTN have a funded clinical research, business, training and dissemination plan (“funded network”), others operate informally with the aspiration to become funded CTN (“non funded network”).

Funded networks are generally supported by national or international peer reviewed funding (for example from HRB, Science Foundation Ireland (SFI), Horizon 2020). They involve CIs from different institutions, one of whom takes the lead role.

In Ireland, the HRB funding for clinical trial networks supports network and clinical trial activities (for at least one multi-centre trial). Network activities include network governance and management, business development and planning, training, outreach and dissemination. Clinical trial activities, on the other hand, are specific for each clinical trial.

In general, funded networks operate as unincorporated entities (they are not a legal entity) and therefore rely on the academic institutions of the CIs to enter into contracts with each other and other third parties.

Funded networks are generally governed by a funding contract between funder and lead academic institution and a (subsidiary) collaborative contract between academic institutions accepting funding to deliver on the network activities and/or clinical studies.

CTN agreements are very important documents not only because they are legally binding but also because they describe the collaborative, regulatory and funding framework of the network and the clinical trials activities, they provide clarity on the governance and management arrangement including parties’ roles, responsibilities and obligations in relation to the network activities and funding, and they set the terms of the cooperation (approach to publications and intellectual property (IP)).

The Contracts and Legal WG have identified the following contractual challenges in contracting for CTNs.

2.4.2.1 Hospitals and Clinical Trial Network Agreements

Hospitals and their personnel play a very important role in clinical trial networks. However, to date, hospitals have not been a party in CTN agreements and therefore their role is not taken into account and captured in network governance and management arrangements, budgetary requirements and plans for distribution of funding. The absence of such a fundamental party in the network agreement represents a risk for the network ability to deliver on the clinical study activities. This leaves the lead institution with a potential contractual and financial exposure of not being able to deliver on contractual obligations set in the funding agreement.

Recommendations:

Academic sector should engage with the health sector to explore/agree approval requirements, terms and a contractual framework for setting up networks.

Funders should consider this approach and introduce a requirement that any hospital or other health organisations involved in a CTN becomes a signatory in the network agreement.

2.4.2.2 Clarify the Distinction between Network and Clinical Trial Activities

Clinical trial activities relate to the planning, conduct and oversight of clinical trials. CTN activities, on the other hand, relate to the implementation of the network governance and management plan, business plan, training, outreach and dissemination. The distinction between these two types of activity is not always immediately clear in grant applications, awards and funding terms and conditions. This can lead to a lack of clarity on insurance requirements, indemnities and liabilities.

Recommendations:

Grant applications and associated funding awards should make a distinction between the activities and terms and conditions for clinical trials activities and network activities. It is recommended that CTN agreements are used for governing network activities, leaving the governance of clinical trials to CTAs. Each network should consider whether it is appropriate and helpful to include clauses which relate to IP and publication in the network agreement as well as in CTA to ensure a consistency of approaches across the network.

2.4.2.3 Clarify the Role of Clinical Research Facilities/Centres (CRF/Cs) in Network Clinical Trial Activities

The role played by CRF/Cs in assisting network clinical trial activities is often unclear in grant applications and funding awards. In particular, it is unclear whether the role of the CRF/C is to support a specific clinical trial/work package involving an investigator affiliated to the CRF/Cs academic institution, or to provide generic clinical research support to the network, regardless of the affiliation of the CIs. Academic institutions are therefore often confused on their role in a network agreement and this confusion causes contractual delays.

Recommendation:

Grant applications should specify/clarify the role of any CRF/Cs involved in network and clinical trial activities in the context of the applicable work package.

2.4.2.4 Put in Place a Contractual Framework Governing Non-Funded Networks

Non funded networks, to date, appear to have no contractual framework governing their activities. In the absence of clarity around scope of activities, terms of cooperation, governance and management arrangements, contracting activities around clinical trials and funding can be very time consuming and there is a potential unintentional exposure for all parties involved.

Recommendations:

The academic sector should engage with the health sector to highlight the benefits of having contractual clarity and exploring/agreeing a contractual approach for non- funded networks.

As a light touch, an example would be that consideration could be given to the signing of a short letter of agreement which refers to pre-defined national principles.

2.5 RESOURCING OF SPONSORSHIP

Co-Chairs of the WG: *Michèle Cunnane (HRB CRCI), John Gaffney (NUIG from March 2018), Dr Fiona Manning (RCSI –until March 2018)*

Contributors: *Dr Caitriona Creely (HRB), Sandra Hammersley (UL), Dr Fionnuala Keane (HRB CRCI), Clare Lehane (UCC), Tony Malone (UCD), Liam Ramsell (UCC), Gareth Shaw (UCD), Jeremy Towns (CRDI/TCD)*

Observers: *Dr Natalie Cole (HSE), Sarah Dever (HSE)*

The infrastructure to deliver multi institutional clinical studies continues to evolve, along with the tools to identify the cost of undertaking such activities.

Academic institutions incur significant costs in the delivery of sponsorship responsibilities. These costs are associated with the delivery of sponsorship oversight, contracts, pharmacovigilance, monitoring, auditing, insurance cover, data management and protection, pharmacy and training.

To promote and sustain clinical studies it is therefore important that the costs associated with these activities are assessed, included in funding applications and funded.

To achieve this the CECR action plan set the objective to develop and agree costing and funding models for regulated and unregulated studies that support the engagement of hospitals in research and resourcing of academic institutions so that they can fulfil all responsibilities.

The Resourcing of Sponsorship WG set the following objectives:

- Identify a comprehensive list of activities incurred when undertaking clinical research.
- Group costs by direct, enabling and indirect and validate this list across the academic institutions.

Direct Costs, which are study specific costs associated with undertaking a clinical study and should be included in applications to the relevant funder/funding agency.

The HRB CRCI Budget Group, developed a standardised costing model and associated documentation to identify project specific direct costs for clinical research. Refer to HRB CRCI website (<https://www.hrb-crci.ie/>) for tools and documentation.

Indirect Costs, for clinical studies include institutional services and facilities (such as space, electricity, telephone, information technology infrastructures), administrative support and management, (for example human resources, legal, financial and information technology) all of which are complex to measure. In the case of clinical studies, the institutional activities to support and manage the sponsorship of clinical trial also include the delivery of sponsorship oversight, contracts, pharmacovigilance, monitoring, auditing, insurance cover, data management and protection, pharmacy and training. Unlike the United Kingdom, where the indirect cost rate is 120%, in Ireland the costs associated with these additional activities are not covered by the funders' budget contribution for indirect costs which range between 25-

30% of the applicable direct costs. Academic Sponsors are therefore left with a significant funding shortfall which they have to cover from their own funds.

In the absence of a similar approach in Ireland, in order to limit the funding shortfall, the Resourcing of Sponsorship WG proposes the introduction of a new cost category called **Enabling Costs** for sponsorship-related activities. Enabling costs relate to institutional infrastructure and resources which are necessary for the delivery of clinical research. These resources/infrastructures may be shared across different studies but represent a significant cost to an institution to ensure that appropriate sponsorship oversight, governance, regulatory compliance and contracts are in place. Examples of costs falling under these categories are listed in Appendix V of this report.

To ensure that clinical studies are adequately costed and funded, the Resourcing of Sponsorship WG recommends that:

- Institutions adopt the HRB CRCI Budget Group guidelines for the assessment and inclusion of direct costs into funding applications.
- Academic Sponsors assess measurable enabling costs at study planning stage and funders allow their inclusion in grant applications.
- The higher education institutions sector develops a robust model that help academic Sponsors identify and quantify enabling costs.
- The academic sector engages with the health sector to identify the costs sustained by hospitals in the support and conduct of clinical studies and explore models to support these activities.
- The research overhead rate review, which involves funding agencies, government departments and the Irish Universities Association, consider the inclusion of clinical research and a full economic costing model for clinical research is developed.

2.6 CLINICIAN ENGAGEMENT AND SUPPORT

Co-Chairs of the WG: *Dr Fiona Manning (RCSI), Dr David O Connell (UCC)*

Contributors: *Dr Caitriona Creely (HRB), Fiona Cregg (HRB CRCI), Prof Ger Curley (RCSI/Beaumont Hospital), Prof Joe Eustace (HRB CRF, Cork), Prof Mark Sherlock (RCSI/Beaumont Hospital), Prof David Williams (RCSI/Beaumont Hospital)*

Observer: *Dr Natalie Cole (HSE)*

Most clinicians in Ireland have no protected time for clinical research, are under pressure to deliver their clinical duties and have limited time and opportunities to engage in clinical studies. When they engage, they are often unaware of the research supports provided by their affiliated academic institutions, which in turn may not be tailored to address their specific research support needs. Clinicians may not be aware of the institutional risks associated with clinical studies and the importance of contracts to mitigate them. Some clinicians therefore perceive risk assessments and contracting activities as a bureaucratic exercise which limits and slows down clinical research activities. This led to unrealistic expectations regarding contract turn-around times, time-consuming engagements between research support services/contract offices and clinicians and, overall, tension in the system which has a negative impact on the relationships between research support services/contract offices, the academic institutions and hospitals.

The Clinician Engagement and Support WG was tasked to identify and address the challenges faced by clinicians in engaging in research and the challenges of academic institutions to provide research support to clinicians.

The WG engaged with the Royal College of Physicians Ireland (RCPI) to explore the possibility of the inclusion of clinical research as part of the formal training programmes for clinicians and trainees. As it was not possible to achieve this in the timeframe of the CECR initiative, the WG recommended that this possibility is explored further.

2.6.1 Action on Clinician Engagement and Support

To understand the type and level of support that academic institutions currently provide to clinicians and the degree to which the delivery of this support was coordinated within each institution, the Clinician Engagement and Support WG carried out a survey of the support that research offices/support services (RO/RSSs) and clinical research facilities/centres (CRF/Cs) provide to clinicians across the academic sector. They also carried out a survey on a small group of clinicians to understand their perspective on the support available to them and any gaps that need to be addressed. Methodology and detailed findings of the surveys are available in Appendix VI of this report.

This report summarises the surveys' key findings, identifies gaps in the provision of supports and provides some recommendations.

2.6.2 Key Findings and Recommendations

Finding 1: The structures and set up for the provision of support for clinical studies varies from institution to institution. Individual academic institutions have separate RO/RSS functions and CRF/Cs located in different sites/locations. RO/RSS are generally located on the main academic institution's campus and the CRF/Cs are co-located on a hospital site. Institutions which have developed CRF/Cs more recently (such as University of Limerick's Clinical Research Support Unit and Crumlin Hospital's Children's Clinical Research Unit) have developed a model, where the functions/services of both RO/RSSs and CRF/Cs are co-located.

Across the sector, a need to improve the interaction between CRF/Cs and RO/RSS to provide an enhanced, better coordinated and more streamlined support service to clinical researchers was identified.

Recommendation 1: The services delivered by RO/RSS and CRF/Cs are in many ways complementary and interdependent. It is, therefore, important that these services maintain strong communication links, are well coordinated, shared procedures, and hold regular meetings with clinical researchers. Ideally, RO/RSS would have a physical presence (manned office) at the local hospital site (perhaps as part of the CRF/C) to provide better engagement between the two functions and within the clinical studies community.

A clinical research support role/function as described in Appendix VII should be in place to facilitate the delivery of better coordination.

Finding 2: The types and accessibility of specialised clinical studies support expertise and services varied across the CRF/Cs. This was linked to the model of HRB core funding for a number of CRF/Cs, which supports additional central resources. The other CRF/Cs receive funding primarily from their institutions to support these central activities, but the level of funding is not uniform across all.

Recommendation 2: It is recommended that core funding is provided to all CRF/Cs.

Finding 3: Access to support in specific areas of clinical research expertise (for example data management, pharmacovigilance, monitoring, budgeting for clinical studies, research design) is not equally available in all academic institutions.

Recommendation 3: Develop a model for delivering specialised clinical study expertise and support in the area of data management, research design and pharmacovigilance and support via a shared service model. To limit costs, Institutions should consider sharing specialised resourced in these areas of support.

Finding 4: There are gaps of expertise and support in the areas of preparation of clinical research grant applications, clinical research project management (including project planning and set up/initiation), projects coordination, clinical study administration and post award administration.

Recommendation 4: It is recommended that new support roles should be put in place to deliver on the following functions:

- Be the central point of contact for researchers, who provides expert, specialised

guidance and advice on pre and post award processes and activities, including signposting to relevant services and personnel where applicable. Coordination of post-award activities relating to sponsorship requirements, study start-up, “green-lighting” and running the study.

- Working on behalf of the chief investigator (CI), support study start-up activities as well as activities continuing after study completion. Facilitate the interaction between relevant departments/function to co-ordinate study start-up activities including award sign-off and grant set up, contracts/agreements, preparation of ethics/regulatory submissions, recruitment of staff and study initiation activities. Post study activities include final reporting requirements and management of on-going activities such as biobanking and archiving.

NOTE: The above roles may be combined into a single job function or be delivered as a number of different functions depending on individual institutions requirements (as described in the clinical research support role in Appendix VII and recommendation 3).

- In the area of pre-award administration, deliver hands-on assistance in the preparation of grant applications, including coordination of partners and completion of forms. In the area of post-award administration, deliver assistance in the preparation of ethics applications and support in the paperwork required for grant set-up. This support allows the CI to focus on activities in which he/she can deliver greater added value.
- Act as a point of contact for institutions with national clinical studies infrastructures.
- Dedicated central research nurse pool to support individual projects (for example contract for a specific time as per project requirements).

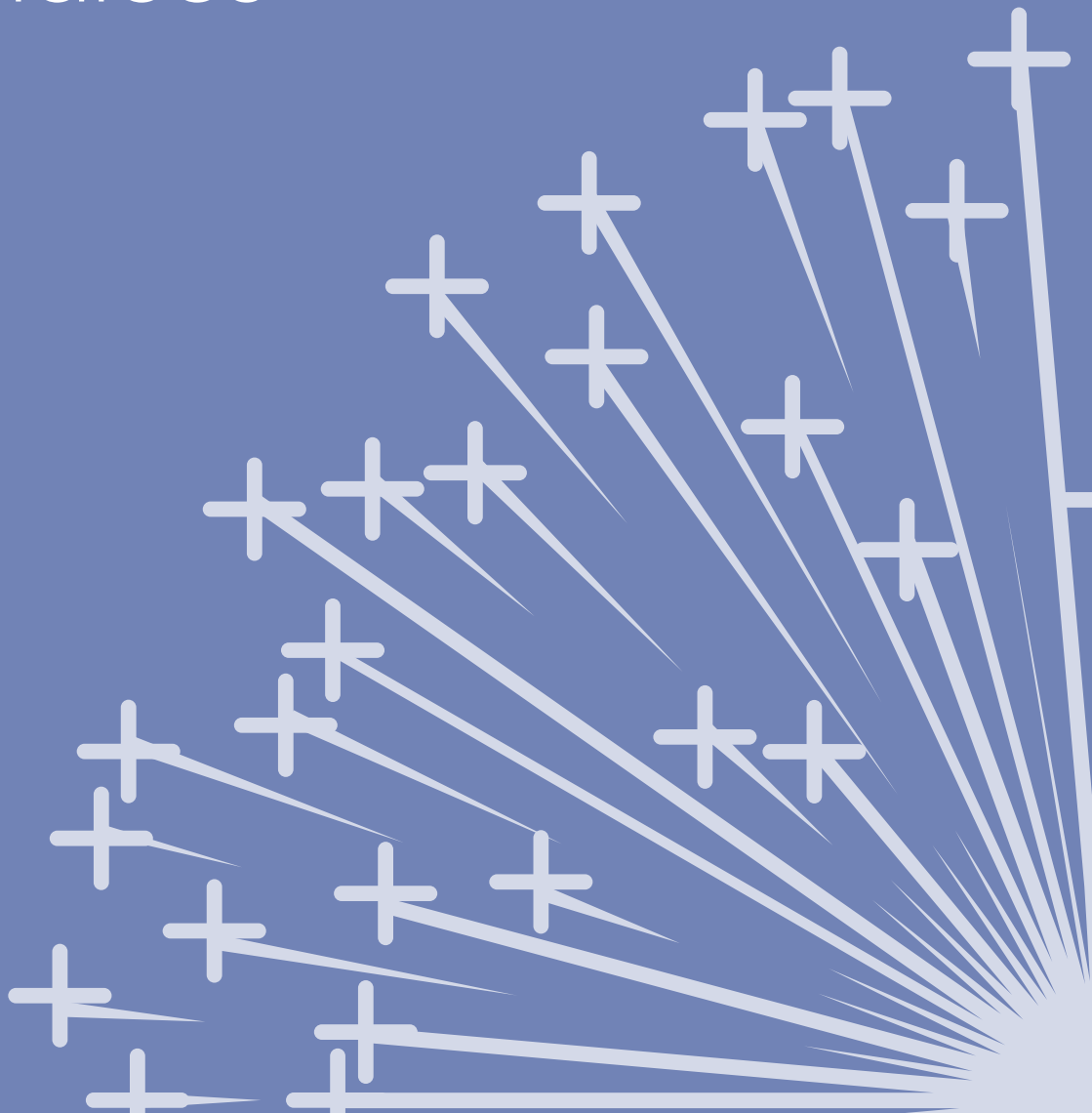
Finding 5: Clinicians at all stages of their careers are interested in getting involved in/carrying out studies. However, clinician feedback indicated that getting started in studies is often very challenging, in particular for clinicians at early career stage. The lack of protected time for research, seed funding and or the availability of resources such as research nurses on an ad hoc basis or for short term projects, makes it challenging for clinicians to engage in studies. Clinicians who are heavily involved in clinical studies abroad see the lack of research support as a significant disincentive to returning to Ireland.

Recommendation 5: The health and academic sectors, in consultation with clinicians, should consider an organisational and funding model that support the engagement of clinicians in clinical studies.

Finding 6: There is a lack of awareness amongst the clinical study community of research supports available from their academic institutions.

Recommendation 6: Working closely with the proposed clinical research support function (Appendix VII), it is recommended the development of a clinician-championed, peer to peer communication/engagement plan locally at individual institutions/hospitals. This communication strategy will inform the clinical research community of the supports (personnel and expertise) and the associated processes for delivery that are available to them.

Appendices



Principles of Good Practice and Collaboration Arrangements to Deliver Clinical Research Across the Academic and Health Sectors

1. Management of Staff Engaging in Clinical Research

In order to ensure effective research governance, the cooperation between the academic and health sectors should provide arrangements governing the management and accountability of staff engaging in research activities across the two sectors.

To achieve this, it would be helpful to define and put in place the terms of engagement of employees of one sector in research activity involving resources of the other. The Governance and Leadership WG therefore propose the following:

- Academic institution employees who do not hold a joint appointment with the hospital, including employees of institutions where the academic institution is not affiliated to any hospital, and require access to patients or patient data, or organs, or tissues are required to work under the direct supervision of a hospital employee to ensure that the academic institution employees under his/her supervision adhere to the agreed principles of cooperation, relevant policies and guidance. Any such activity (such as access to patients, patient data and materials) should require approval by the hospital and the employer academic institution and the commitment of the chief investigator (CI) to comply with the hospital's policies and procedures.
- Hospital employees with no contractual relationship with the academic institution and leading research under the auspices or in the name of the academic institution should be in possession of a research affiliation or other contract issued by the academic institution and agreed by the investigator and the employer hospital.

The affiliation of hospital employees with an academic institution for the conduct of research is not intended to be a contract of employment and therefore would not necessarily provide any entitlement to remuneration. However, to be effective, it would be helpful if the CI and his/her employing hospital sign a legally binding agreement with the relevant academic institution, in which they commit to comply with the terms and conditions of the research affiliation. This includes;

- a) Ensuring institutional policies, procedures, and quality systems are in place in the host.
- b) Collaborating hospitals and institutions should develop and share a joint database of researchers.
- c) Holding a contract of employment with the hospital and a contract of affiliation with the academic institution.
- d) Holding a contract of employment with the academic institution and working under the supervision of a hospital employee.

Documentation on individuals, activities and supervisory roles falling outside payroll records would help identify and address any existing gap in state indemnity and commercial insurance cover and ensure that the institutions involved maintain the necessary oversight.

2. Responsibilities

There should be clear and documented designation of responsibility and accountability with clear lines of communication between all those involved in research (for example individuals and organisations). Communication pathways should be clear in terms of who, what, when and how with documented roles and responsibilities.

Research team members' accountability should be clearly agreed between themselves, the investigator and their employer(s) and the WG would like to see this fully documented.

Clarity on responsibilities should apply to all clinical research activities, including those relating to data protection.

A proposed sample template for documenting the division of responsibilities among institutions and individuals involved in a clinical research study is available in annex 3 of this document.

2.1 Role and Responsibilities of Chief Investigators

All research involving hospital's resources or patients should have a designated hospital investigator. This individual should be of consultant status or equivalent.

The investigator should have adequate training and experience and should always be made aware of and be asked to accept his/her duties and responsibilities, including the supervision of the study team, which may include academic institution employees who are part of it.

The CI is the overall lead researcher for a research project.

In addition to his/her responsibilities as a member of the research team, the CI is responsible for the overall conduct of a research project, including providing reassurance to the Sponsor that;

- The research plan takes into account any relevant systematic reviews, other research evidence and research in progress.
- The research project makes effective use of patients, service users and involves the public where appropriate.
- The research plan is scientifically sound, safe, ethical, legal and feasible and remains so for the duration of the research, taking account of any developments while the research is ongoing.
- The research plan or protocol has been submitted for appropriate independent expert ('peer') review and revised in light of that review.

- If expected or required, the research plan has been submitted for review by and obtained approval from a research ethics committee and any other relevant approval bodies.
- Everyone involved in the conduct of the research is qualified by education, training and experience, competent and fully trained in study procedures to discharge their roles in the project.
- The information given to potential participants is in a suitable format and is clear and relevant to his/her participation in the research.
- He/she will adhere to the agreed arrangements for making information about the research publicly available before it starts (unless a deferral is agreed by or on behalf of the research ethics committee).
- He/she will adhere to the agreed arrangements for making data and tissue accessible, with adequate consent and privacy safeguards, in a timely manner after the research has finished.
- He/she will start the research only when the sponsor has confirmed that everything is ready for it to begin and all necessary approvals are in place.
- He/she will adhere to the agreed procedures and arrangements for reporting (such as progress reports, safety reports) and for monitoring the study, including conduct, participant safety and well-being and ongoing benefit risk assessment in light of adverse events or other developments.
- That he/she will adhere to the agreed arrangements for making information about the findings of the research available, including, where appropriate, to study participants.
- That he/she will familiarise himself or herself with and adhere to any applicable requirements, procedures and timelines imposed by their employer and any other institutions involved in the clinical study.

With exception of commercial research, the Sponsor of a clinical study should have a contract of employment or a legally binding affiliation with the CI.

2.2 Role of Students in Clinical Research Studies

Students should not normally take the role of CI at any level of study, as this function should be undertaken by supervisors or course leaders. Undergraduate students should only conduct clinical studies that involve direct patient contact where there are no study procedures or interventions that require medical qualifications and where on-site supervision arrangements fully mitigate any risks. Exceptions can be made for an experienced care practitioner or manager undertaking an educational qualification for continuing professional development or a doctoral-level study while employed by a healthcare provider or an academic institution, or for a researcher undertaking a doctoral-level study in receipt of a fellowship.

3. Research Approval

Research should only take place when all required ethics, regulatory and institutional approvals/authorisations are in place.

Hospitals and institutions should ensure that their employees are aware of and adhere to the requirements and procedures for obtaining approval to start their study.

Before the academic institution or the hospital approves a study, the employee or affiliate who is leading the study (the CI) should commit to adhere to the study governance policies of the hospital and/or the academic institution as appropriate.

Hospital approval: Formal and explicit approval by the hospital should be required before research can begin when one or more of the following scenarios apply:

- The study is a medium or high-risk intervention.
- Employees of the hospital are researchers (except where such hospital employees are submitted as subjects through another hospital).
- The study requires access to resources, facilities or services of the hospital.
- The study requires access to patients for which the hospital has responsibility, their relatives or carers. This includes access to confidential information, tissues, organs or fluids (whether taken specifically for research, taken from material that is surplus to clinical requirements, or archived material).
- The study requires a student/clinical placement in the hospital.
- The study requires the secondment of an academic institution employee in the hospital.

Academic institution approval: This should be obtained before the academic institution or hospital staff holding a contract of affiliation with the institution commences a study involving patients or staff of the hospital, or tissues or records associated with patients of the hospital or involves access to hospital resources or facilities. Other approval requirements may apply on a case-by-case basis depending on the institutional requirements.

Sponsorship approval and other requirements are covered in the next section of this document.

4. Sponsorship of Clinical Trials

The EU Directive on Clinical Trials (2001) requires there to be a Sponsor for all clinical trials falling within its scope.

‘Sponsor’ means the organisation taking on ultimate responsibility for the initiation, management (or arranging the initiation and management), insurance cover and financing (or arranging the financing) of that study.

All clinical research studies should have a named institutional Sponsor. The role of Sponsor, however, cannot be assumed by default in virtue of the institutional role as employer of the investigator wishing to undertake a clinical study.

The academic institution and the hospital should have the possibility to assess their ability to deliver on the Sponsor role. To this end, the WG recommend the development of a transparent, clear and well-communicated sponsorship review process.

Since risks cannot be pre-empted without assessment, any clinical study involving patients, patient data or material should be registered, and risk assessed.

Institutions taking on the role of Sponsor should put in place procedures for managing sponsorship applications, ensure that sponsorship risks and mitigation plans are documented and used to inform sponsorship decisions. Sponsorship decisions should also be documented and justified.

A clear and well-communicated sponsorship governance plan would ensure that sponsorship oversight is delivered throughout the lifecycle of the study.

Guidance documents and training (as necessary) would assist all stakeholders involved. To facilitate the engagement of institutions with hospitals for the approval and conduct of clinical research, it would be helpful if each party would identify a local point of contact and communicate it to the other.

When an academic institution sponsors a study, the hospital that employs the study's investigator, hosts the clinical study and is responsible for the clinical care of the study subjects, should cooperate with the academic Sponsor and their respective responsibilities should be agreed and documented.

An important role that hospitals play in academic sponsored clinical research studies is to ensure that the study's clinical concept, methodology and risk/benefit analysis are adequate. Hospitals should help academic Sponsors ensure that study plan are feasible and sustainable. The hospital may decide to delegate these responsibilities to the study's CI or his/her head of department but the ultimate responsibility for these activities should rest with the hospital.

The acceptance of the academic sponsorship role should be subject to the academic institution being satisfied with factors such as the following:

- Study's plan, including funding,
- Study's risk benefit analysis,
- Sponsorship risk assessment and mitigation plan,
- Confirmation of sponsor insurance,
- Acceptance by the hospital of the responsibilities delegated to it and documented in

the division of responsibility table of the clinical trial agreement between the academic institution and the hospital,

- Any other condition that may apply on a case by case basis.

Sample sponsorship approval pathway, governance and management arrangements for academic sponsored clinical research are described in the sponsorship governance and management plan included in Appendix III of this document.

5. Research Management and Governance

The hospital and the academic institution should make available to each other relevant information needed to ensure proper governance of research. This may include information on activities concerning both the academic institution and the hospital and may include:

- Research funding applications, particularly to ensure respective proper costs are included in applications, and that research award income is distributed appropriately and in accordance with other relevant agreements between the parties.
- Sponsorship applications and reports.
- Research publications and other forms of output.
- Relevant audit reports.
- Relevant research activity and any untoward incident or misconduct.

The academic institution and the hospital should nominate an institutional point of contact(s) for sharing documentation in relation to the above and other, as needed.

In sharing information within this context, the academic institution and the hospital should take due regard to and respect the legal restrictions on data protection and confidentiality and avoid breaches of confidentiality and ensure compliance with the Freedom of Information Act 2014.

The academic institution and the hospital should ensure that their staff abides by the GDPR, and the Health Research Regulations 2018 and that personal data is stored and managed according to legal obligations.

6. Ownership and Management of Intellectual Property

Intellectual property (IP) should be managed in accordance with the National IP protocol 2016⁵.

⁵ **Inspiring Partnership – the National IP Protocol 2016**, Knowledge Transfer Ireland
<http://www.knowledgetransferireland.ie/ManagingIP/KTI-Protocol-2016.pdf>

Experience and expertise for protecting and managing IP are generally only available in the academic institution. It may therefore be in the interest of the partnership of the academic institution with affiliated hospitals that the institution take the lead in the protection and commercialisation of IP arising from clinical studies. To implement this, it would be necessary that hospitals would agree that the IP arising from the study activities of the clinicians with a contract of affiliation with the academic institution is owned by that institution. Hospitals would therefore assign to their affiliated institutions their ownership of such IP to the greatest extent possible. Institutions would enter into such assignment agreements as necessary with affiliated investigators and hospitals to give effect to this arrangement. In turn, institutions would evaluate and, where appropriate, manage, prosecute and commercialise the IP for the shared benefit of the academic institution, the CI and the hospital. Hospitals would also provide access to any background IP owned by it that may be necessary for the affiliated academic institution to conduct the relevant research activities.

Institutions would be responsible for taking all decisions regarding filing, patenting and commercialisation of any IP but, without prejudice to the foregoing, would use all reasonable endeavours to prosecute through to registration all relevant patent applications filed by it and would similarly use all such reasonable endeavours to procure a fair market value in respect of any commercialisation of the IP.

All business development and commercialisation activities in relation to any IP developed would be led and negotiated by the institutions.

Following deduction of reasonable and verifiable costs and expenses incurred by the academic institution in the protection, maintenance, business development, marketing and commercialisation of the IP any remaining financial benefits would be shared, at the agreed proportion, by the academic institution, the CI and the hospital.

7. Finances - Costing of Research, Distribution and Transfer of Funding

The hospital and the academic institution should work together to ensure that legitimate costs incurred by both parties are incorporated into all contracts and/or research grant applications where applicable.

8. Liability, Insurance and Indemnity

The academic institution and the hospital should ensure adequate insurance or indemnity is in place before any clinical research can commence.

The State Indemnity Guidelines (SIG) document, Insurance and Indemnity arrangements for Patient Focused Clinical Research between DSA Healthcare Enterprises and Academic Institutes, developed by the State Claims Agency (SCA) (who manage the Clinical Indemnity Scheme and General Indemnity Scheme) in consultation with the CECR partner institutions, provides guidelines on insurance cover for clinical research. The document clarifies what the state insurance (such as the Clinical Indemnity Scheme) covers and conditions associated with it. The document also clarifies what additional commercial insurance cover is needed by academic institutions, when sponsoring clinical trials. The complete SIG is available on the SCA website (<http://stateclaims.ie/resources>).

9. Research Contracts and Agreements

Institutions and hospitals should agree their respective responsibilities with regard to the drafting, negotiation and execution of research agreements with collaborators and funders (for example public and private funding bodies and industry) which relate to research study activities of any joint employees and affiliates.

Both the academic institution and the hospital should have the opportunity to review and, when appropriate, approve funding and collaboration agreements (including terms and conditions) relating to research activities which fall under the scope of this document.

Neither the hospital nor the academic institution should sign a contract that commits services or resources provided by the other, without the prior agreement of the other party.

To ensure a greater efficiency and quality of contracting activities across the clinical research system, it is recommended that the academic and health sectors adopt as many template contracts for clinical trial agreements, collaborative clinical research programmes and data and material sharing agreements, as possible.

Templates developed under the CECR initiative are available at <http://crdi.ie/corporate-enabling-of-clinical-research>.

10. Code of Conduct for Clinical Research, Competence, Quality and Integrity

Contract of engagement of employees of one sector in research activity involving resources of the other should be subject to terms and conditions, including compliance with the hospital's and academic institution's policies, procedures and codes of conduct for research studies.

Irish institutions have committed to comply with principles of the National Policy Statement on Ensuring Research Integrity in Ireland (2014)⁶ and recommend that they are adopted also by Irish hospitals.

Collaborating hospitals and institutions should then work to agree a common code of conduct for clinical research and procedure for handling research conduct in keeping with national and European guidance.

All personnel involved in managing and conducting a research project should be competent and possess the education, training and experience to perform their tasks under the supervision of a suitably qualified person.

CI and Sponsors should be knowledgeable about any applicable legislation and guidance relating to the management and conduct of research studies.

⁶ **National Policy Statement on Ensuring Research Integrity in Ireland 2014**, Irish Universities Association <https://www.iua.ie/publication/view/national-policy-statement-on-ensuring-research-integrity-in-ireland/>

Research should be designed, reviewed, managed and undertaken in a way that ensures integrity, quality and transparency of data.

The design and procedures of the clinical study should be clearly described and justified in a research proposal or protocol, and, where applicable, conform to a standard template and/or specified contents.

A risk benefit analysis should always be carried out prior to the commencement of a clinical study. Written evidence should be provided (for example in the protocol) that any anticipated benefits for the study participants outweigh any foreseeable risks and inconveniences and all risks have been mitigated as far as possible.

The academic institution and the hospital of the CI and/or members of the research team should encourage a high-quality research culture by:

- Ensuring employees are supported in and held to account for conducting research in a professional manner, including research integrity.
- Ensuring effective management of employees and their work, including employees' safety, well-being, work environment and facilities.
- Ensuring adequate financial planning, management and calculation of costs in support of financial probity.
- Ensuring agreements with partners (such as funders, Sponsors, collaborators, commercial partners, network members and integrated boards) and employees are in place to document accountability and division of responsibilities, including arrangements for any IP arising from the research.
- Ensuring researchers understand and discharge their responsibilities fully.
- Following good human resources practice, to ensure that employees are qualified, trained and competent and that written procedures and supervision support accountability and effective collaboration.
- Encouraging care with financial resources; raising awareness of the wider environment within which health and social care research is conducted; and bridging any gap between employees' current competence and the competence needed for their work.
- Taking proportionate and effective action in the event of errors or breaches or if misconduct or fraud are suspected.
- Promoting a culture of continuous improvement which encourages open and honest reporting of errors and incidents and therefore supports safety and improves the quality of health outcomes.

- Ensuring appropriate individual learning and competence. This includes acknowledging existing experience, qualifications and skills, rather than just training personnel. Training should have measurable learning outcomes that are competence-based and directly linked to the competencies demanded by the employee's role and procedures (such as standard operation procedures) relevant to that role.

- Ensuring that CIs and their teams are made aware of and comply with the principles outlined in this document.

For interventional studies:

- Any deviation from normal treatment or investigations should be adequately justified by the available information (including evidence from previous research).

- The protocol and the participant information leaflet should explain any special arrangements, that may be required/apply after the research intervention period has ended (for example continuing or changing the treatment, care or other services that were introduced for the purposes of the research).

- The duty of care owed by healthcare providers continues to apply when their patients and service users take part in research. A healthcare professional retains responsibility for treatment, care or other services given to patients. If an unmanageable conflict arises between research activities and patient interests, the duty to the participant as a patient should prevail.

11. Clinical Research Support

The provision of support pre and post study initiation is subject to the availability of support staff and therefore advance planning and timely engagement are required. When the study is operational the support is subject to funding being available on a cost recovery basis.

To fulfil their role CRF/C clinical research nurses (CRNs) should, subject to the necessary agreements, be allowed access to the hospital patients, data and facilities for the sole purpose of supporting the study as specified in the clinical protocol and under the supervision of the study's CI.

Information on research nurses' activities, training, mentoring and supervisory arrangements should be documented and made available to hospitals and clinicians by the employing CRF/C.

12. Research Dissemination

Information about clinical research activities and outputs should be disseminated broadly and responsibly to the scientific community and the public in order to contribute to the general body of scientific knowledge and, ultimately, to the public health. At the same time, it is important that the academic institution and the hospital work together to ensure that provision of this information is done in such a way as to avoid breaches of confidentiality and the GDPR, to protect IP and to comply with the Freedom of Information Act 2014.

13. Patient Involvement

The participation of patients in the development of research, including the design, management, conduct and dissemination of research, public engagement and setting research priorities helps health research deliver greater impact.

Patients and other interested parties should be given the opportunity to participate and contribute to the design, management, conduct and dissemination of research.

14. Access to Patients, Patient Material and Information

14.1 Right to Privacy and Informed Consent

Research participants should be afforded respect and autonomy.

Where there is a difference between research procedures and standard practice, research participants should be given information to understand the distinctions so that they can make an informed choice, unless a research ethics committee agrees otherwise. Study participants' consent should be freely given, explicit, voluntary and informed. Where consent is refused or withdrawn, this should be done without reprisal toward ongoing clinical care.

All information collected for or as part of a clinical study should be recorded, handled and stored appropriately and in such a way and for such time that it can be accurately verified, while maintaining confidentiality of individual research participants.

Data and tissue collections should be managed in a transparent way that demonstrates commitment to their appropriate use for research and appropriate protection of data protection, privacy and other applicable laws.

The GDPR and the Health Research Regulations 2018 govern information obtained by the hospital for the provision of healthcare.

Researchers must obtain written informed explicit consent from patients or use other lawful authorisations before involving them in the clinical study. They must ensure that the consent process is documented in patient records.

Researchers who are not hospital employees should have direct access to patient records only under the supervision of a hospital employee.

The transfer of data from the academic institution to the hospital (and vice versa) should be subject to the approval of the academic institution and the hospital and the terms of a data transfer agreement between the academic institution and the hospital.

The academic institution and the hospital should agree a formal mechanism to enable the transfer of confidential information between themselves when appropriate with due regard to the requirements for consent and data protection.

Institutions and hospitals should ensure that they have organisational and technical measures in place to protect personal data.

14.2 Collection, Use and Storage of Human Tissue, Fluids and Organs

The use of human tissue, fluids and organs of patients under the care or previously under the care of the hospital, whether obtained specifically for research, obtained from material that is surplus to clinical requirements, obtained from archived sources within the academic institution or the hospital, or obtained at post mortem, should be governed by policies agreed by the academic institution and the hospital.

The academic institution and the hospital should ensure that their employees are aware of and abide by these policies.

The academic institution and the hospital should ensure that any human tissue, fluids and organs taken, stored or used for research is only done with the explicit consent of the patient.

The academic institution and the hospital should agree a formal mechanism to enable the transfer of tissues and samples between themselves and ensure that tissue samples are not exported from the hospital unless with the consent of the patient.

The academic institution and the hospital should develop a common policy on handling human tissue for research, to ensure that such research, whether undertaken by the academic institution or hospital employees, is subject to proper governance procedures.

The academic institution and the hospital should safeguard the confidentiality of all information relating to consent. For this purpose, each party should have standard operating procedures to ensure that all information, including the informed consent, is provided in confidence and is kept confidential and only disclosed where required by law.

The academic institution and the hospital should maintain appropriate licenses, quality management systems and standard operating procedures relating to the storage of human tissue, coding and recording systems and maintain a robust audit trail.

15. Health and Safety

15.1 Occupational Health

The academic institution and the hospital should ensure that all employees are aware of and abide by codes of practice, guidelines and policies on health and safety of both parties. Responsibility for adherence to any such codes or guidelines lies with the CI and the institutional leads for health and safety.

15.2 Pharmaceuticals

All medicines used for research must be stored and dispensed through the hospital's pharmacy or through alternative arrangements explicitly agreed with the hospital's head of pharmacy

services.

The academic institution and the hospital should consider entering into a service level agreement for the provision by the hospital's pharmacy department of professional advice in respect of the academic institution's pharmacy responsibilities as sponsor of clinical trials involving investigational medicinal products.

For specific studies involving the academic institution as Sponsor, the hospital's role as a participating site would be covered by a model agreement for non-commercial research or other appropriate agreement. All studies sponsored by the academic institution that require pharmacy services above and beyond those of a participating site should be covered by an appropriate agreement detailing the responsibilities of each party with respect to the study.

Agreed Terminology

Clinical Trial: is, in scientific terms, a type of research in which the study determines and assigns which subject receives an intervention of interest. 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 1 - the Competent Authority (in Ireland the HPRA –formerly the IMB) uses the term “Clinical Trial” in a more restricted sense, in that they only apply it to trials that fall under the HPRA jurisdiction (in general, trials of an investigational medicinal product or of a prototype medical device). For other studies which do not fall under their remit but would in a general scientific sense be defined as a clinical trial, they use the term “non-interventional trial”.

Figure 1: Classification of Patient Focused Research

Patient Focused Research						
	Interventional			Non-Interventional		
Type	IMP (1A/B)	Devices (2A/B)	Other (3)	Observational (4)	Bio Banking	Data Analysis

Investigational Medicinal Product (IMP) 1A/B: A regulated clinical trial is a clinical trial that falls under the remit of the competent authority, (in Ireland the HPRA). This typically involves an IMP that falls under the IMP regulatory framework (SI 190/2004) which makes compliance with a specific set of good clinical practice guidelines (ICH GCP), a legal requirement for study conduct. In the case of multi-site trials, the legislation governing regulated clinical trials also allows for a single ethics opinion from any one of several nationally recognised ethics committees within the country.

Devices 2A/B - A Regulated Clinical Investigation: By historical usage clinical trials of medical devices are referred to as clinical investigations, especially in regulatory discussions. A regulated clinical investigation is therefore a study of a medical device that falls within the clinical trials regulatory framework for medical devices, and therefore in Ireland, is carried out under HPRA/NSAI Regulations. Note that these regulations are distinct to, but in many areas overlap with, the regulations that govern IMP trials. However, unlike trials falling under SI 190/2004, there is no provision for a single national ethics opinion for multi-site regulated clinical investigations.

Note 2 - where the regulated intervention is a hybrid between an IMP and a device the HPRA will determine which regulation applies based on the primary mode of action.

Other 3 - A Non-Regulated Clinical Trial: Is a clinical trial that does not fall within a specific legislative framework. They do not therefore have specific legislation governing their conduct and therefore need to obtain local ethics approval for each site, any additional approvals required as per the site approval, and must comply with data protection legislation and with the general scientific principles as laid out in ICH GCP (unlike regulated trials these are not legally binding for non-regulated trials). However, if the study does not comply with ICH GCP, the data cannot be used for regulatory submission.

Observational 4 - An Observational Clinical Study: Is a non-interventional study or one where the assignment of an intervention is not decided by the protocol but takes place as part of standard therapeutic practice and is completely independent of the study. All observational research needs to obtain local ethics approval for each site, any additional approvals required as per the site approval, and must comply with data protection legislation and the general scientific principles as laid out in ICH GCP (but unlike regulated trials these are not legally binding for non-observational studies). However, if the study does not comply with ICH GCP, the data cannot be used for regulatory submission.

Note 3 - An observational study merely means that the factor or intervention that the principal investigator is interested in studying is not controlled or directly applied as part of the study. The term 'observational study' does not by itself imply that the study is either non-invasive or low risk. Types of Observations are included in Annex A.

Post-Marketing Studies: Commercial companies often fund and/or conduct additional studies on approved marketed products being used clinically in their approved indication (Phase IV studies). Post marketing studies can range from simple Phase IV studies to HPRA regulated clinical investigations. When a post marketing study is proposed, clarification should be sought from the HPRA as to the regulatory requirements.

Intellectual Property (IP): means inventions, designs, specifications, information, techniques, know-how, patents, formulae, data, methods, processes, copyright, trademarks, software, materials, moral rights, database rights, confidential information or any other intellectual or industrial property right of any nature whatsoever in any part of the world (including the right to apply for the foregoing).

ROLES

Sponsor: In academic research the Sponsor is the academic institution which has ultimate legal responsibility for compliance with the regulation that governs clinical research. The Sponsor (institution) will identify a Sponsor Signatory Official (SSO) who has ultimate responsibility for managing institutional research risks.

Sponsorship Oversight Committee (SOC): The scope of the SOC is to help the Sponsor Signatory Official (SSO) (Chair of the SOC) to make sponsorship decisions and deliver institutional oversight of clinical research. The members of the SOC could include the Sponsor Office(r) (whose role is described below) and other members of staff with relevant expertise

within the academic institution.

The SOC would review sponsorship applications and provide advice on sponsorship matters. The SOC also reviews ongoing clinical trials and ensures that they progress as planned or any plan for deviation is appropriate.

The advice of the SOC on sponsorship decisions is documented in a report. The report can be used to support any subsequent decision taken by the Sponsor and, if appropriate, could be shared with the investigator.

The SOC may escalate decisions relating to very high-risk studies or reports of patient harm to the institutional body responsible for managing institutional risks.

Sponsor Office(r) (SO): The SO would have an institutional operational and advisory role that helps the Sponsor ensure any risk associated with clinical research is understood, accepted and adequately managed. These activities require clinically competent unbiased assessments and decisions. To avoid conflict of interest, the SO's line manager should be the SSO. The SO is the primary point of contact for chief investigator (CI) on regulatory matters and would act as the institutional point of contact for sponsorship applications and approvals. To help prepare for sponsorship applications, the SO would provide clarity and guidance to the CI on how to complete the clinical study registration form (CSRf) and how to undertake a risk/benefit analysis. The information provided in the CSRf is intended to help the institution assess the risks associated with the study in question and ensure that the study has adequate insurance/indemnity cover. The SO would assist the CI in finalising the protocol to ensure that it is regulatory compliant. Depending on institutional choice the SO role may be fulfilled by an individual or a team of individuals led by the SO.

It is proposed that the SO's responsibilities may include the following:

- Ensure the feasibility of a study.
 - Ensure that the CI has undertaken a clinical risk/benefit analysis that will inform the institutional decision on sponsorship approval.
 - Make a sponsorship risk assessment and put in place a mitigation plan including oversight requirements (for example monitoring and pharmacovigilance plan).
 - Document (and clarify the rationale for) the monitoring plan. The monitoring plan includes monitoring methods, responsibilities and requirements.
 - Ensure that a clinical risk assessment and mitigation plan is in place before the recruitment of patients.
 - Approve and sign off the protocol and any other study document (as applicable).
 - Ensure compliance with approval requirements (such as institutional, HPRA, ethics, legal, hospitals and Data Protection Authority).
 - Ensure compliance with Good Clinical Practice (GCP).

- Routine and non-routine reporting to the head of research and others (as appropriate).
- Escalate as appropriate issues that may highlight a risk to patient safety/data quality or to the reputation of the academic institution.
- Oversight and support of the quality management systems in place in institutional clinical research facilities/centres (CRF/Cs).
- Ensure many tasks are assigned/delegated and clearly understood.

The SO may delegate some of his/her tasks to the institutional clinical research facility/centre (CRF/C) (for example quality and regulatory affairs manager, project manager, data manager, clinical trial monitors and/or pharmacovigilance manager, where applicable). However, ultimate responsibility for the tasks listed above would rest with the SO. During the implementation of the study, the SO would advise the academic institution regarding the status of studies as follows:

Routine Reporting: To fulfil ethical and regulatory safety reporting requirements the SO should review and present details on the progress of studies at the SOC meetings, which are held at a time interval defined by the academic institution.

Non-Routine Reporting: The SO would be in contact with the SSO and/or the SOC (as deemed appropriate) on a regular basis regarding a range of issues related to clinical research. Where any issue is identified that may seriously impact on patient safety, data quality, or cause reputational damage to the academic institution, the SSO would be immediately notified by telephone or e-mail (as appropriate). The SSO may further escalate any issue to the academic institution senior executive team and/or management team (operations), academic institution President or other representatives (as applicable) at his/her discretion. The SSO may defer any issue that could present a serious risk to patient safety/data quality or to the reputation of the academic institution to the institutional body responsible for managing institutional risk.

The SO would report to the SOC and his/her role in the decision on sponsorship approval is at the discretion of the SSO.

Investigator: The authorised health care professional responsible for the conduct of a clinical trial at a trial site.

Sub Investigator: Authorised health care professional working alongside the principal investigator at a trial site.

Principal Investigator (PI): Where a trial is conducted by a team of individuals at a trial site, the principal investigator is the responsible leader of that team.

Chief Investigator (CI): The CI is primarily responsible for the concept, rationale, study design and the day-to-day running of the study in accordance with the approved protocol and in keeping with GCP. The CI is also responsible for the study's risk-benefit analysis which is required to support the sponsorship decision on the study proposal.

Study Planning Group (SPG): It is proposed that the SPG would be a multidisciplinary group made up (as required) of personnel from clinical research support, quality and regulatory affairs manager, project manager, data manager, clinical trial monitor, pharmacovigilance, research offices/support services (RO/RSS) and contract/legal. Led by the SO, the SPG would be responsible for the preparatory work, which precedes the commencement of a clinical trial. The SPG also reviews the documentation of sponsorship applications before it is submitted to the SOC for review/approval. The role of RSSs and/or CRF/Cs would be to help the CI in applying for funding and provide guidance in budgeting and operational tasks of a clinical research study. CRF/Cs may also provide sponsorship services under the oversight of the SO. Specific functions proposed for the RSS are outlined in the approval pathways described in Section 4 of this document.

Study Operational Team (SOT): The SOT includes the investigator and the clinical staff involved in the study. Once the study is approved and up and running, the SOT becomes responsible for the operation of the study under the oversight of the SO.

Contract Officer (CO): The designation of CO refers to the individual in the organisation who would be responsible for drafting, reviewing and negotiating clinical research collaboration and CTAs. The CO would work with the insurance point of contact to ensure that clinical trials insurance/indemnity are adequately addressed in the clinical research agreements. The title of this role may vary in institutions and the roles and responsibilities may be spread across different areas of the institution.

Insurance Point of Contact (IPoC): The IPoC would be an individual responsible for submitting the relevant documents to the insurer to ensure that appropriate insurance/indemnity is in place. As each trial/study is reviewed on a case by case basis it may be necessary on occasion to arrange for additional premium cover. The IPoC should liaise with the RO/RSS and CI and/or SO on any feedback received from the insurer.

Data Safety and Monitoring Committee (DSMC): The proposed DSMC would be a group of experts with no relationship to the study operational team who monitor patient safety and treatment efficacy data while a clinical trial is ongoing. The requirement for a DSMC should be assessed by the SOC on the basis of the study's risk level.

Funders: The funder is 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 take responsibility before the regulated or non-regulated trial begins. In some instances where there is academic funding, assessment of the scientific quality of the research proposal will take place.

Co-ordinator/Lead: The co-ordinator or lead is the organisation that acts as the contract and funding liaison point for the funder in the event that multiple organisations are applying collectively (as a consortium) for grant funding. The co-ordinator lead may decide to assume the role of Sponsor via the contractual arrangements between the consortiums, but the roles are neither identical nor mutually exclusive.

The Site: The site is the organisation providing access to the patient/study subjects and retaining responsibility for the care of the participants to whom they have a duty of care.

Annex A: Patient Focused Research Classification Table	
1 Investigational Medicinal Product	
1A	<p>This is regulated clinical trial where an academic institution assumes the role of legal Sponsor. It is envisaged that over time, this classification will be further sub-divided into three categories:</p> <ol style="list-style-type: none"> 1. Pharma 2. Biologics 3. Cell tissue <p>At present we will remain with just one classification.</p>
1B	<p>This is regulated clinical trial where the academic institution has a role but where a third party assumes the role of Sponsor (for example pharma company)</p>
2. Medical Device for example from a bandage to a cardiac stent - key issue is the risk classification of the device trial, is it assessed as Class I, II, III (with III being the device investigation with the highest risk).	
2A	<p>This is a regulated clinical investigation where an academic institution assumes the role of Sponsor.</p>
2B	<p>This is regulated clinical investigation where an academic institution has a role but where a third party assumes the role of Sponsor (for example device co).</p>
3. Non (Competent Authority) regulated clinical trials such as trials of nutritional products, exercise programs, care pathways.	
3A	<p>This is a non- regulated clinical trial where an academic institution assumes the role of academic Sponsor.</p>
3B	<p>This is non- regulated clinical trial where an academic institution has a role but where a third party assumes the role of academic Sponsor.</p>
4. Non-interventional/observational studies which can be further sub-divided into I, II and III, where observational studies involve:	
<ul style="list-style-type: none"> • no invasive testing • low risk tests, such as blood or swabs • an invasive clinical procedure such as lumbar puncture and tissue biopsy or could be secondary data analysis 	
4A	<p>This is an observational study where an academic institution assumes the role of academic Sponsor.</p>
4B	<p>This is an observational study where an academic institution has a role but where a third party assumes the role of academic Sponsor.</p>

Sample Methodologies and Tools to Help Deliver Academic Sponsorship Responsibilities

1. A Sample Model for the Governance and Management of Sponsorship Responsibilities

1.1 Rationale

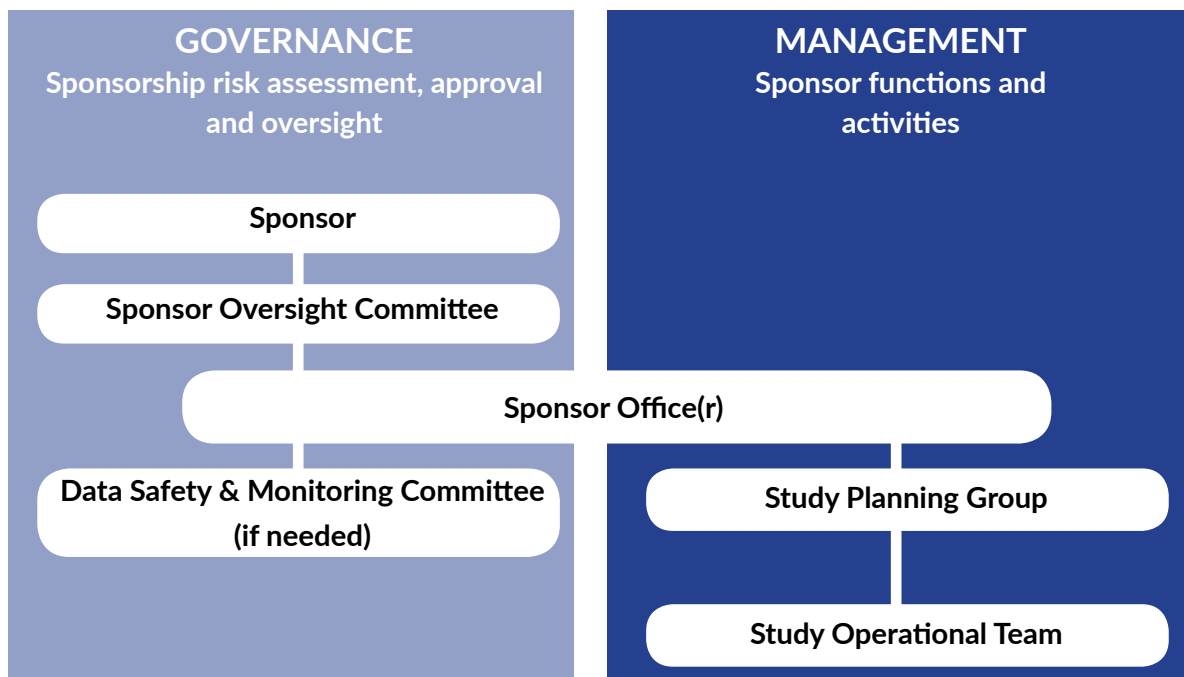
Sponsorship of clinical trials is a significant undertaking for academic institutions as it requires compliance with regulatory requirements; risk assessment and management; sustainability planning; coordination of institutional functions responsible for regulatory compliance, pre and post-award research support, clinical research management and support, pharmacovigilance, governance, insurance/indemnity, contract and legal.

It is therefore important that academic institutions put in place a management and governance structure that ensures that sponsorship decisions are well informed, sustainable and aligned with institutional strategies. At the same time, sponsorship oversight should be planned and put in place for the duration of the study. The level of oversight required during the implementation of the study should be assessed carefully and be commensurate with the study's risk level.

1.2 Governance and Management Structure

The following diagram represents a sample model of governance and management structure for the delivery of the sponsorship role for clinical studies. Individual functions may be used as required.

Diagram 1: Sponsor Governance and Management Structure



1.3 Roles and Responsibilities

The roles and responsibilities of the individuals and groups involved in the delivery of the sample governance and management model are outlined below. This model is not intended to be prescriptive and if adopted, consideration should be given to how it could be adapted to any pre-existing organisational structure, governance, management arrangements and availability of resources.

Sponsor: In academic research the Sponsor is the academic institution which has ultimate legal responsibility for compliance with the regulation that governs clinical research. The Sponsor (institution) will identify a Sponsor Signatory Official (SSO) who has ultimate responsibility for managing institutional research risks.

Sponsorship Oversight Committee (SOC): The scope of the SOC is to help the Sponsor Signatory Official (SSO) (Chair of the SOC) to take sponsorship decisions and deliver institutional oversight of clinical research. The members of the SOC could include the Sponsor Office(r) (whose role is described below) and other members of staff with relevant expertise within the academic institution.

The SOC would review sponsorship applications and provide advice on sponsorship matters. The SOC also reviews ongoing clinical trials and ensures that they progress as planned or any plan for deviation is appropriate.

The advice of the SOC on sponsorship decisions is documented in a report. The report can be used to support any subsequent decision taken by the Sponsor and, if appropriate, could be shared with the investigator.

The SOC may escalate decisions relating to very high-risk studies or reports of patient harm to the institutional body responsible for managing institutional risks.

Sponsor Office(r) (SO): The Sponsor Office(r) (SO) would have an institutional operational and advisory role that helps the Sponsor ensure any risk associated with clinical research is understood, accepted and adequately managed. These activities require clinically competent unbiased assessments and decisions. To avoid conflict of interest, the SO's line manager should be the SSO. The SO is the primary point of contact for chief investigator (CI) on regulatory matters. He/she would be the institutional point of contact for sponsorship applications and approvals. To help prepare for sponsorship applications, the SO would provide clarity and guidance to the CI on how to complete the clinical study registration form (CSRF) and how to undertake a risk/benefit analysis. The information provided in the CSRF is intended to help the institution assess the risks associated with the study in question and ensure that the study has adequate insurance/indemnity cover. The SO would assist the CI in finalising the protocol to ensure that it is regulatory compliant. Depending on institutional choice the SO role may be fulfilled by an individual or a team of individuals led by the SO.

It is proposed the SO's responsibilities may include the following:

- Ensure the feasibility of a study.
- Ensure that the CI has undertaken a clinical risk/benefit analysis that will inform the institutional decision on sponsorship approval.
- Make a sponsorship risk assessment and put in place a mitigation plan including oversight requirements (for example monitoring and pharmacovigilance plan).
- Document (and clarify the rationale for) the monitoring plan. The monitoring plan includes monitoring methods, responsibilities and requirements.
- Ensure that clinical risk assessment and mitigation plan is in place before the recruitment of patients.
- Approve and sign off the protocol and any other study document (as applicable).
- Ensure compliance with approval requirements (such as institutional, HPRA, ethics, legal, hospitals and Data Protection Authority).
- Ensure compliance with Good Clinical Practice (GCP).
- Routine and non-routine reporting to the head of research and others (as appropriate).
- Escalate as appropriate issues that may highlight a risk to patient safety/data quality or to the reputation of the academic institution.
- Oversight and support of the quality management systems in place in institutional clinical research facilities/centres (CRF/Cs).
- Ensure many tasks are assigned/delegated and clearly understood.

The SO may delegate some of his/her tasks to the institutional clinical research facility/centre (CRF/C) (for example quality and regulatory affairs manager, project manager, data manager, clinical trial monitors and/or pharmacovigilance manager, where applicable). However, ultimate responsibility for the tasks listed above would rest with the SO. During the implementation of the study, the SO would advise the academic institution regarding the status of studies as follows:

Routine Reporting: To fulfil ethical and regulatory safety reporting requirements the SO should review and present details on the progress of studies at the SOC meetings, which are held at a time interval defined by the academic institution.

Non-Routine Reporting: The SO would be in contact with the SSO and/or the SOC (as deemed appropriate) on a regular basis regarding a range of issues related to clinical research. Where any issue is identified that may seriously impact on patient safety, data quality, or cause

reputational damage to the academic institution, the SSO would be immediately notified by telephone or e-mail (as appropriate). The SSO may further escalate any issue to the academic institution senior executive team and/or management team (operations), academic institution President or other representatives (as applicable) at his/her discretion. The SSO may defer any issue that could present a serious risk to patient safety/data quality or to the reputation of the academic institution to the institutional body responsible for managing institutional risk.

The SO would report to the SOC and his/her role in the decision on sponsorship approval is at the discretion of the SSO.

Chief Investigator (CI): The CI is primarily responsible for the concept, rationale, study design and the day-to-day running of the study in accordance with the approved protocol and in keeping with GCP. The CI is also responsible for the study's risk-benefit analysis which is required to support the sponsorship decision on the study proposal.

Study Planning Group (SPG): It is proposed that the SPG would be a multidisciplinary group made up (as required) of personnel from clinical research support, quality and regulatory affairs manager, project manager, data manager, clinical trial monitor, pharmacovigilance, research offices/support services (RO/RSS) and contract/legal. Led by the SO, the SPG would be responsible for the preparatory work, which precedes the commencement of a clinical trial. The SPG also reviews the documentation of sponsorship applications before it is submitted to the SOC for review/approval. The role of RSSs and/or CRF/Cs would be to help the CI in applying for funding and provide guidance in budgeting and operational tasks of a clinical research study. CRF/Cs may also provide sponsorship services under the oversight of the SO. Specific functions proposed for the RSS are outlined in the approval pathways described in Section 4.

Study Operational Team (SOT): The SOT includes the investigator and the clinical staff involved in the study. Once the study is approved and up and running, the SOT becomes responsible for the operation of the study under the oversight of the SO.

Contract Officer (CO): The designation of CO refers to the individual in the organisation who would be responsible for drafting, reviewing and negotiating clinical research collaboration and CTAs. The CO would work with the insurance point of contact to ensure that clinical trials insurance/indemnity are adequately addressed in the clinical research agreements. The title of this role may vary in institutions and the roles and responsibilities may be spread across different areas of the institution.

Insurance Point of Contact (IPoC): The IPoC would be an individual responsible for submitting the relevant documents to the insurer to ensure that appropriate insurance/indemnity is in place. As each trial/study is reviewed on a case by case basis it may be necessary on occasion to arrange for additional premium cover. The IPoC should liaise with the RO/RSS and CI and/or SO on any feedback received from the insurer.

Data Safety and Monitoring Committee (DSMC): The proposed DSMC would be a group of experts with no relationship to the study operational team who monitor patient safety and treatment efficacy data while a clinical trial is ongoing. The requirement for a DSMC should be assessed by the SOC on the basis of the study's risk level.

1.4 Oversight Required During the Implementation of Clinical Trials

To deliver sponsorship responsibilities for clinical research, a Sponsor institution should ensure adequate oversight is provided on an ongoing basis. To achieve this, the Sponsor should consider putting in place a project management plan, medical oversight and safety monitoring. The project management plan would ensure that the study's activities are compliant with the protocol and overall clinical trial objectives while adhering to all related regulatory and ethics requirements.

In the proposed model, whereby the SO is responsible for the implementation of Sponsorship responsibilities, the SO may delegate some of the tasks of the project management plan to one or more members of the SPG. However, in this sample governance structure, ultimate responsibility for implementation of the project management plan would rest with the SO.

Based on the risks and complexity of a trial, the Sponsor may appoint a DSMC. The DSMC may include but is not limited to personnel with clinical and scientific expertise in the clinical aspects of the disease/patient population being studied, including study conduct and methodology.

The role of the DSMC would be to provide expert, independent, scientific and/or medical oversight and continuing benefit/risk monitoring. To this end, the DSMC would hold regular meetings (example quarterly) to assess the progress of the clinical trial, including data safety and the critical efficacy endpoints at intervals as appropriate. Examples of items to cover would include study status, withdrawal data, deviations and impact with respect to endpoints/analysis, safety listings/signals and data listings.

Upon completion of each review, the DSMC would recommend to the Sponsor (SOC via SO) whether to continue, modify, or stop a trial.

To inform the DSMC's safety monitoring, the study operational team(s) may be delegated to complete reports, which are signed off by the CI before being collated and issued to the DSMC. The DSMC may request clarifications within a given time.

The European Medicines Agency has issued guidelines⁷ on data monitoring committees.

2. A Sample Classification Based Sponsorship Approval and Planning Requirements for Clinical Trials

2.1 Approach to Classification

To streamline and better inform sponsorship approval and planning processes, this document proposes a sample methodology to help identify the approval and planning requirements of a clinical study depending on where it falls in the classification below (Table 1).

⁶ **Guideline on Data Monitoring Committees 2005**, European Medicines Agency
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003635.pdf

Table 1: Classification of Study

Sponsorship Risk level	Non-interventional - observational		Interventional - non-regulated				Interventional - regulated						
	Non-invasive testing (data collection only)	Low risk tests, such as blood, swab, etc.	Invasive clinical procedure such as lumbar puncture, tissue biopsy, CT Scans etc.	Non-IMP (food, herbal products homeopathic products, etc)		Device		IMP	Device				
				CE marked product	Non-CE marked product	Non-invasive / potentially harmful Intervention	Non-invasive / potentially harmful Intervention						
Low	Low	Low	Medium	Low	Trial of nutritional products, exercise programs, care pathways etc.	Trial of food intervention involving multiple blood tests taken from an intravenous cannula, other non-medical intervention that may have physiological effects	Trial of invasive or potentially harmful non-IMP intervention (e.g. food allergy testing with the possibility of provoking a severe reaction such as anaphylaxis).	invasive / potentially harmful Intervention	Non-invasive intervention	Non-invasive / potentially harmful Intervention	Non-invasive intervention	High/regulated	High/regulated
Low	Low	Medium	Medium	Medium	High	High	High	Medium	Medium	High	Medium	High/regulated	High/regulated

The HPRRA decision tree below (Table 2) can help determine whether an IMP study is regulated or non-regulated.

Table 2: HPRRA Decision Tree

A	B	C	D	E
A clinical trial of an IMP?				Non-Interventional Clinical Trial?
Is it a medicinal product (MP)? ¹	Is it not a medicinal product?	What effects of the medicine are you looking for?	Why are you looking for those effects?	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 you answer no to <u>all</u> the questions in column A, the activity is not a clinical trial on a MP	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 <u>all</u> the questions in column C the activity is not a clinical trial under the scope of the Directive 2001/20/EC	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 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
If you answer yes to any of the questions below go to column B	If you answer no to this question below to go column C	If you answer yes to any of the questions below go to column D	If you answer yes to any of the questions below go to column E	E.1 Is this a study of one or more medicinal products, which have a marketing authorisation in the Member State concerned?
A.1. Is a substance ² 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 administered for a medicinal purpose? A.3 Is it an active substance in a pharmaceutical form?	B.1. Are you only administering any of the following substances? Human whole blood ³ Human blood cells Human plasma A food product ⁴ (including dietary supplements) not presented as a medicine A cosmetic product ⁵ 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 ⁶ of the medicine D.2 To ascertain or verify/compare the safety of the medicine?	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 the current practice and is not decided in advance by a clinical trial protocol? ⁷ E.4 Is the decision to prescribe a particular medicinal product clearly 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 is replaced by Article 1.1 of Directive 2004/27/EC, which provides the definition of “medicinal product” which applies for the purposes of Directive 2001/20/EC.

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 Somatic cell therapy medicinal products use somatic living cells of human (or animal) origin, the biological characteristics of which have been substantially altered as a result of their manipulation to obtain a therapeutic, diagnostic or preventative effect (in humans) through metabolic, pharmacological and immunological means.
- v 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.
- vi 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 to keep them in good condition, change their appearance or correct body odours.
- vii 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.
- viii Assignment of patients to a treatment group by randomisation planned by a clinical trial protocol cannot be considered as current practice.

2.2 Study Classification

The classification of the study by the SO according to the criteria outlined in table 1 is based on information provided by the CI in the clinical study registration form (Annex 1).

The CSRF form would serve as a first notification by a CI to his/her institution of his/her plan to undertake a clinical research project.

Its completion would be required for any interventional, observational, epidemiological or physiological research study, which involves humans, human tissue and/or data, regardless of the source of funding, use of Investigational Medicinal Product (IMP) or device.

This form would be completed as early as possible and submitted to the academic institution’s SO together with any other documentation available at that time (for example study protocol, grant application, patient information leaflet, investigators brochure and risk benefit analysis documents).

2.3 Classification-Based Risk Assessment, Risk Management and Approval Requirements

Table 3: Classification – Based Risk Assessment, Risk Management and Approval Requirements

	Non-interventional - observational				Interventional - non-regulated				Interventional - regulated	
	Non-invasive testing (data collection only)		Invasive clinical procedure such as lumbar puncture, tissue biopsy, CT Scans etc.		Non-IMP (food, herbal products homeopathic product, radiotherapy, surgery research studies etc)		Device		IMP	Device
	Low risk tests, such as blood, swab, etc.	Low risk	Trials of nutritional products, exercise programs, care pathways etc.	Trials of food intervention involving multiple blood tests taken from an intravenous cannula, other non-medical intervention that may have physiological effects	Trial of invasive or potentially harmful non-IMP intervention (e.g. food allergy testing with the possibility of provoking a severe reaction such as anaphylaxis).	CE marked product	Non-CE marked product			
Sponsorship Risk level	Low	Low	Medium	Low	High	Medium	High	Medium	High/regulated	High/regulated
Requirements										
Approval by SOC	No*	No*	Yes	No*	Yes	Yes	Yes	Yes	Yes	Yes
Sponsorship Risk assessment	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Risk-benefit analysis (procedures must be within PI's competencies and must be indemnified by medical malpractice insurance /indemnity).	No	No	Yes (testing must be clinically appropriate e.g. undergoing biopsy for clinical reasons, additional biopsies taken for research)	No	Yes - to ensure that the risk / benefit ratio is positive	Yes - to ensure that the risk / benefit ratio is positive	Yes - to ensure that the risk / benefit ratio is positive	Yes - to ensure that the risk / benefit ratio is positive	Yes - to ensure that the risk / benefit ratio is positive	Yes - to ensure that the risk / benefit ratio is positive
ICH-GCP risk assessment	No	No	No	No	No	No	No	No	Yes	Yes
Risk management plan	No	No	No	No	No	No	Yes	No	Yes	Yes
Pharmacovigilance Plan	No	No	No	No	No	No	No	No	Yes	Yes
Contract with clinical site	to be assessed	to be assessed	to be assessed	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Green light	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Monitoring	No	No	No	No	Yes - risk based	Yes - risk based	Yes - risk based	Yes - risk based	Yes - risk based	Yes - risk based

*Observational studies are only reviewed by the SOC in certain cases (e.g. concerns regarding the suitability/research experience of the investigator, concerns regarding the affiliation of the investigator, concerns that funding may be inadequate or inappropriate, IP concerns relating to the data or study output, concerns regarding investigator co-operation with commercial interests or a possible conflict of interests). (Table Source: CECR Sponsorship and Quality Working Group).

In the proposed sponsorship management model, the SO would review the form and any documents provided with it to classify the study and its risk level according to the criteria outlined in Table 3.

Depending on the first-tier risk level in table 3, the SO would determine whether confirmation of insurance/indemnity, sponsorship risk assessment and approval are required.

The SO may share the clinical study registration form (and any documentation associated with it) with the SCA and/or the academic institutions underwriters.

Annex 5 (classification-based post-approval requirements table) provides details of standard sponsorship requirements depending on where the study fits in the classification. The tables included in Annex 5 provide details of the regulatory/non-regulatory requirement and guidance documents which need to be adhered to for the running of the studies depending on where they fit in the classification, for example whether they are non-interventional studies (Table 7), interventional studies on IMP's excluding devices (Table 8), or interventional studies on devices (Table 9).

3. A Sample Risk Informed Sponsorship Approval and Oversight Requirements

Sponsorship risk assessments and mitigation plans can help make an informed sponsorship decision and managing institutional risks.

This section of the document describes sample methodology and tools that could be used to identify, document and, if possible, manage institutional risks so that sponsorship decisions are well informed and transparent.

3.1 Sponsorship Risks and Classification

There are two key areas of risk that a Sponsor must consider: quality/system/study -related risks as detailed in ICH GCP (R2) and study sponsorship risks.

a) Quality/System -Related Risks

The regulatory framework (ICH GCP EG (R2) Section 5.0 Sponsor responsibilities) stipulates that the Sponsor quality management system should use a risk-based approach including risk identification, risk evaluation, risk control, risk review, risk communication and risk reporting methods. Given this requirement, the institution must ensure competent and experienced staff are in place to manage quality/system-related risks; apply the ICH-GCP methodology to risk assessment; ensure that trials are well designed; and adequate quality standards and systems are in place to manage key operational areas (IMP, pharmacovigilance, monitoring, data management/reporting, record management, governance, facilities, standard operation procedures (SOPs), computerised systems, personnel and vendors). This process is mandated for HPRA-regulated studies and may be applied (at the discretion of the sponsor) to non HPRA-regulated high-risk studies. In general, these processes do not need to be applied to low or medium risk studies.

b) Study Sponsorship Risks

Sponsorship risks are study specific and may be dependent on one or more of the following factors:

- The complexity of the trial (for example multisite, including international and non-EC sites).
- The experience of the CI and the study operational team.
- The type of intervention.
- The type and source of the IMP.
- The classification of the device.
- The market readiness of the device (authorisation stage).
- The availability of funding and the funding source.
- The financial resources to support the trial.
- The involvement of high-risk patient populations (new-born and pregnant women).
- The involvement of vulnerable patient populations (terminally ill, patients with intellectual disability).
- The involvement of a non-CE marked device.
- Conflict of interests.
- Inadequate insurance/indemnity cover.
- Other issues that may influence or inform the decision to sponsor a study.

These risks are not always manageable. It is therefore important to assess them in the specific context of each study to decide on whether the overall level of risk that may have been identified is acceptable. Institutions may have different risk tolerance/acceptance and therefore treatment of such risks will be institution dependent.

Since these types of risks cannot be pre-empted, it is important that institutions are informed of all clinical research activities undertaken by affiliated staff, so that they can be properly classified, and their risk level assessed.

The notifications would be made via submission of a completed CSRF (Annex 1).

The information provided in the CSRF is intended to help determine where the study fits in the classification and its risk level. Depending on the risk level (low, medium, high) the SO, who in the management model proposed in this document is responsible for managing the sponsorship approval process, can determine whether the study can proceed without further assessment (low risk observational studies) or whether a sponsorship risk assessment (SRA) is needed (medium-high risk studies).

It is proposed that each institution undertaking clinical research would maintain a risk register

of all clinical research activities under their remit. This register should contain a high-level view of the study classification and the assigned risk of the study (low, medium, high, very high). The register would track the risk assigned at the sponsorship approval stage and may not necessarily match the in-depth study risk assessment level assigned by the study management group. A macro view of the all institutional clinical research activity (regulated and non-regulated) provided by such a risk register can facilitate an effective risk management approach for clinical research in the institution and enable appropriate assignment of resources commensurate to risk.

3.2 Sponsorship Approval Requirements

The sample approval requirements of the proposed sponsorship management plan depend on the study's first tier risk level:

- Low risk studies - the SO can approve a low risk study to proceed without SOC review.
- Medium risk studies (example low-level intervention) - CI is required to complete a risk benefit analysis, which can be included in the protocol or supplied as a separate document. The SO then completes a Sponsorship Risk Assessment Form (SRAF) (Annex 2) and submits it to the SOC together with the study protocol (or equivalent) and the risk benefit analysis. If the SOC agrees that the study is medium risk, the SOC approves the study, subject to green light. The requirement for a clinical site agreement should be assessed in light of the State Indemnity Guidance (<https://stateclaims.ie/resources>).
- High-risk non-regulated studies - The CI is required to complete a risk benefit analysis (which can be included in the protocol or supplied as a separate document). In consultation with the CI, the SO then completes the SRAF, reviews the risk benefit analysis and considers any risk mitigation activities that may be required to approve sponsorship. In general, high-risk studies, a study risk management plan, greenlight and monitoring to ensure GCP compliance.
- High-risk regulated studies - In addition to the requirement described above for high-risk non-regulated studies, it would be also necessary to include a GCP risk assessment in the documentation that is submitted to the SOC for sponsorship approval. The investigator should provide input to the GCP risk assessment. The GCP risk assessment should be considered by the SOC and help inform the decision to Sponsor the study.

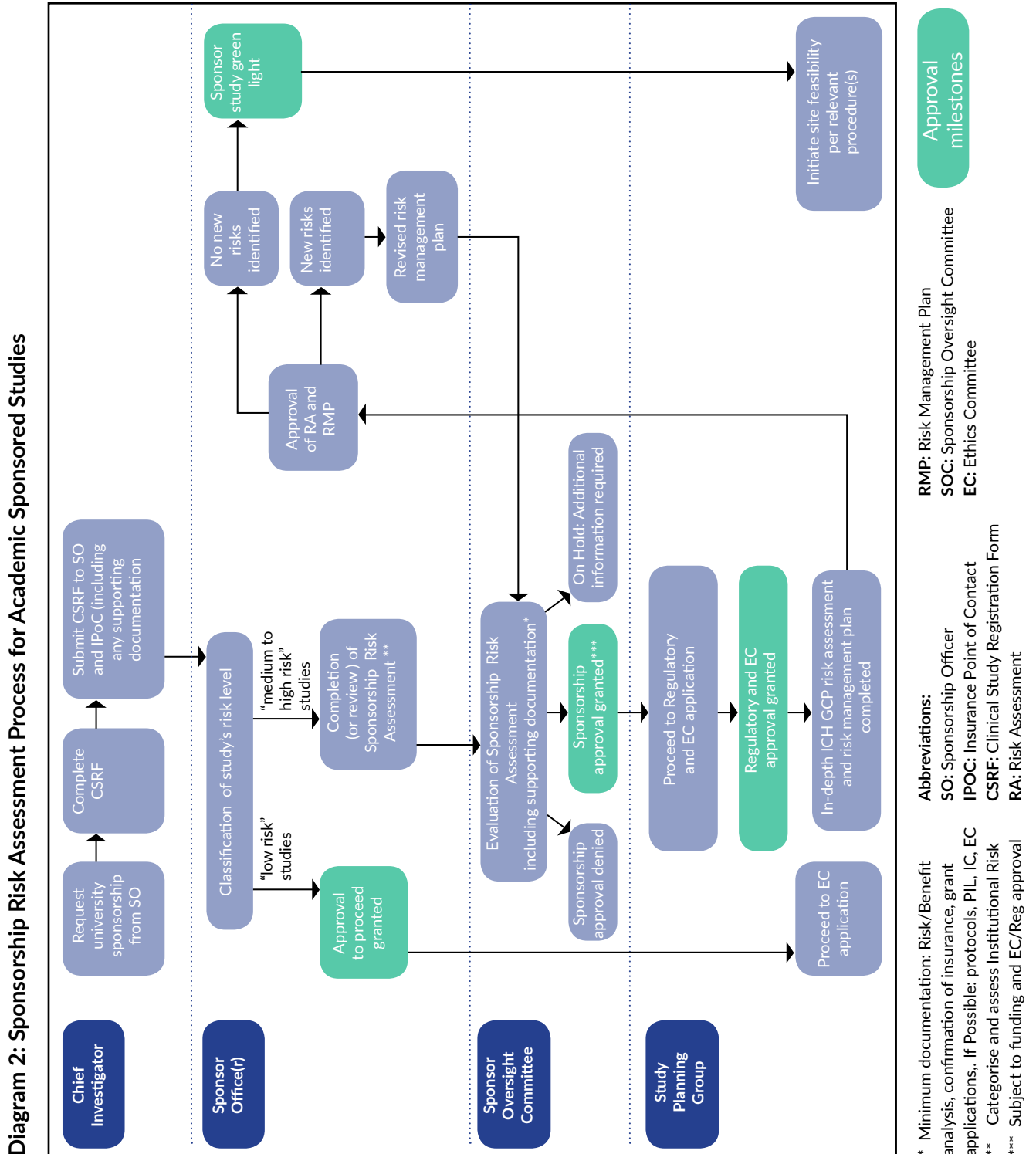
3.3 Sponsorship Risk Assessment – As well as providing the risk benefit analysis when necessary, the CI should provide assistance to the SO in completing the SRAF and confirms (by signing the form) that study specific information included in the form is accurate.

3.4 Division of Responsibilities - The Division of Responsibilities Tables for Medicinal Products and Medical Devices (DORT MP and MD) included in Annex's 3A DORT MP and 3B DORT MD enables the Sponsor to allocate and document the responsibilities of all parties involved

at all stages of a clinical trial. This would be completed by the SO office in consultation with the CI and those with delegated responsibility prior to sponsorship approval being granted.

3.5 Sponsorship Review - Upon its completion, the SRAF and supporting documentation is shared with SOC for review and, if possible, sponsorship approval. The SOC will at this stage complete the Sponsor Oversight Committee Report (SOCR) as per Annex 4.

The diagram below provides an overview of the proposed activities related to sponsorship approval.



3.6 Risk Assessment of Non-Regulated Studies – Challenges, Solutions and Responsibilities

Interventional non-regulated studies (such as academic investigational studies of medical devices) do not fall under the HPRA oversight. However, in some instances, the risks of these studies can be high.

Unless an academic institution has been asked to play any oversight role of a clinical study it is not in the position to ensure that the study's risks are adequately assessed and managed. As a result of this, insurance/indemnity cover may not be adequate, and, in the absence of a clinical trial agreement, the academic institution (who may be the investigator's employer) and clinical sites (where the studies are carried out) may be left with the exposure of not having adequate quality standards and oversight, agreed roles and responsibilities, liabilities and indemnity provisions.

It is therefore proposed that all interventional non-regulated studies follow the same approval pathway of regulated studies so that risks are assessed and, depending on the risk level, oversight requirements as detailed above (such as monitoring) are put in place as per this guidance document.

3.7 Risk Assessment of Device Studies

The differentiation of risk levels in device studies is not solely dependent on where the study fits in the classification (regulated versus non-regulated) but rather on a conjunct assessment of the classification of the device, risk level of the intervention or potential for harm (which should be considered on a case by case basis) and whether the device is/is not CE marked.

If a non-CE marked device is involved, it is highly recommended that the SO seeks the advice of an expert in the regulation of medical devices (possibly external if advice not available in house).

The expert responsibilities include:

- Ensuring that an appropriate clinical evaluation has been conducted and supports the initiation of a clinical investigation.
- Assessing the device development history to confirm that risk management and design control was applied.
- Investigating the manufacturing environment, process and raw materials including supply chain of the planned study devices and where risks are identified, initiate risk reduction for example manufacturing site audit, manufacturing and quality control record audit.
- Conducting medical device regulations and applicable standards training when requested by study operational team

- Reviewing clinical investigation documentation when requested by study operational team.
- Reporting any quality, performance or safety concerns directly to the SO.

If the study involves a CE marked device, the necessity to seek expert advice should be assessed on a case by case basis. Where a CE-marked device is being used within the approved use, no further assessment may be required. Where a device is being used outside of approved use, an expert can provide guidance/advice on the following:

- Assess the clinical risk assessment and management documentation to confirm that off label use of the device does not introduce any unanticipated safety risks.
- Report any quality, performance or safety concerns directly to the SO.

4. A Sample Pathway for Sponsorship Approval and Management of Sponsor Related Activities Which Precede the Recruitment of Patients

In this section, the WG propose sample plans for the approval and coordination of activities which precede the commencement of a clinical study (for example recruitment of patients) in the scenario where a funding application is required (Section 4a) or funding is already in place (Section 4b).

The sample pathways described in this document are not intended to be prescriptive but rather help institutions develop their own institutional pathways, which take into account the institutional organisational and management context.

Ultimately institutional pathways should ensure that sponsorship decisions are informed and timely, that investigators are aware of the process, requirements and timelines of all the activities which precede the commencement of the clinical study and the team contributing to the delivery of these activities (including SO, RSS, CRF/C, CO, IPoC) is well coordinated and fulfils its responsibilities in a timely manner.

4a. Scenario where funding application is required, there is a two stages selection process, SOC approval is required

Table 4: Sample Approval Pathway – Pre-Award

Timeline (days)	Activity
	Pre-Award
	Funding Call Announcement - Expression of Interest Stage
	Research Support Services (RSS): Provides call and guidance documents, including the clinical study registration form (CSRF) (Annex 1).
	Chief Investigator (CI): Confirms intention to apply for funding to RSS and meet with Sponsor Office(r) (SO) to review CSRF and seek advice on the study plan. If the SO anticipates that the study may not obtain insurance/indemnity cover and/or sponsorship approval, the SO highlights the risk to the CI and ensures that sponsorship and insurance/indemnity issues are considered as soon as possible.
	RSS: Clarifies (with human resources) and confirm affiliation of clinician. If the CI has no affiliation, RSS or equivalent share with the CI the institutional guidance document on how to apply for affiliation (if applicable) and clarifies that confirmation affiliation is required for proposal endorsement and sponsorship approval.
	CI: Submits expression of interest to funder.
0	Invitation to submission of full proposal.
5-40	SO: Meets with the CI, communicate/clarify sponsorship review process and discuss/ update content of CSRF. RSS, CRF/C and SO (support roles to be agreed at institutional level): <ul style="list-style-type: none"> • Liaise with CI, provides guidance on full proposal, including completion of budget template. • Provide support in the preparation of the project proposal.
40	CI: Submits funding proposal to funder and copies in RSS and SO and ensures that any collaborator obtain approval from own institution.
40-65	RSS: Review proposal and budget, liaise with CI for any change required and ensure that any partner institution(s) involved in the study approve its/their participation in the proposal and signing a template letter of support. The letter of support includes the role in the proposal, reference to relevant workplans and budget allocation.
40-58	SO: <ul style="list-style-type: none"> • Reviews study plan, the budget (to ensure that the study is sustainable), the CSRF and classifies the study's risk level. • If deemed necessary, shares the CSRF with the IPoC for insurance/indemnity confirmation (45). <p>If the study falls under the low risk category, the SO issues letter of approval to proceed, subject to ethical approval.</p> <ul style="list-style-type: none"> • If the study falls under the medium/high risk category, the SO (in consultation with the CI) completes the sponsorship risk assessment form (SRAF) (Annex 2). • If the SRAF identifies medium risk the SO issues letter of approval to proceed subject to ethical approval and site initiation visit. • If the SRAF identifies high risk and the requirement for SOC approval applies, the SO asks the CI to carry out a risk benefit analysis and with the CI completes division of responsibilities table (DORT) (Annex 3A/B).
45-58	IPoC: <ul style="list-style-type: none"> • Sends CSRF to insurer to determine whether institutional policy would cover the study or additional premium applies. • Upon receipt of response from insurer, liaises with RSS and CI to update budget (if necessary) and with SO to clarify insurance/indemnity.
58	SO: <ul style="list-style-type: none"> • Collate the documentation that informs sponsorship decision (confirmation of CI's affiliation, executive summary of the study and contributors, risk benefit analysis, confirmation of insurance/ indemnity, budget, sponsorship risk assessment). • Share it with the SOC.
60	SOC: Reviews sponsorship risk assessment form and supporting documentation and decides on sponsorship (subject to confirmation of funding, ethics and regulatory approvals).
60	Confirmation of sponsorship approval – communication to PI and SPG.
60-65	CI: Submits full proposal and written confirmation(s) of approval from partner institutions.
65-68	RSS: Endorse proposal.
70	Funding application deadline.

Table 5: Sample Approval Pathway – Post Award

Timeline (days)	Activity
0	Notification of funding
1	RSS: Notify award to Study Planning Group (SPG), CRF/C and RSSs of partner institutions.
2	SO: Organises SPG meeting.
5	RSS: Registers the funding.
7	Study Planning Group (SPG): <ul style="list-style-type: none"> • Reviews CSRF and identifies requirements to be met before the study can commence. • Develops an action plan for the study preparation based on requirements outlined in tables 4-6 of this document.
1-5	SO: Meets with the CI and communicates/clarifies action plan for study preparation, offers support, if necessary.
5-60**	SO/CRF: <ul style="list-style-type: none"> • Liaises with any other CRF/Cs involved in the study to communicate plan and timelines and ensure timeliness and coordination of support activities (40). SO, with CI: <ul style="list-style-type: none"> • Reviews and finalises protocol and other documents required for ethical and regulatory approval (60). **Protocol development is dependent on study complexity and can generally take from 2- 6 months, up to 1 year (for more complex protocols). In these instances, the timelines in this table need to be adjusted. It is therefore important that funders take into account the timing required for protocol development in order to set the terms of the funding agreement which cannot be standardised.
5-100/130	CO: <ul style="list-style-type: none"> • Obtain DORT from SO. • Completes a draft of a clinical trial network, collaboration and/or clinical trial agreement (50). • (If necessary) shares agreement with insurer to confirm cover (50-70). • Circulates agreement(s) to CI and CRF/C for internal review and approval (50-70). • Circulates agreement(s) to academic partners and clinical sites, agreement review and feedback (70-120).
60	CI: submission of documents for regulatory and ethics approval.
120-150	Regulatory (& ethical) approval.
100-130	Execution of agreements.
	SO: Site initiation visit.
150-180	Green light to patient recruitment (subject to regulatory and approval and contract execution).

Diagram 3: Sample Approval Pathway – Pre-Award

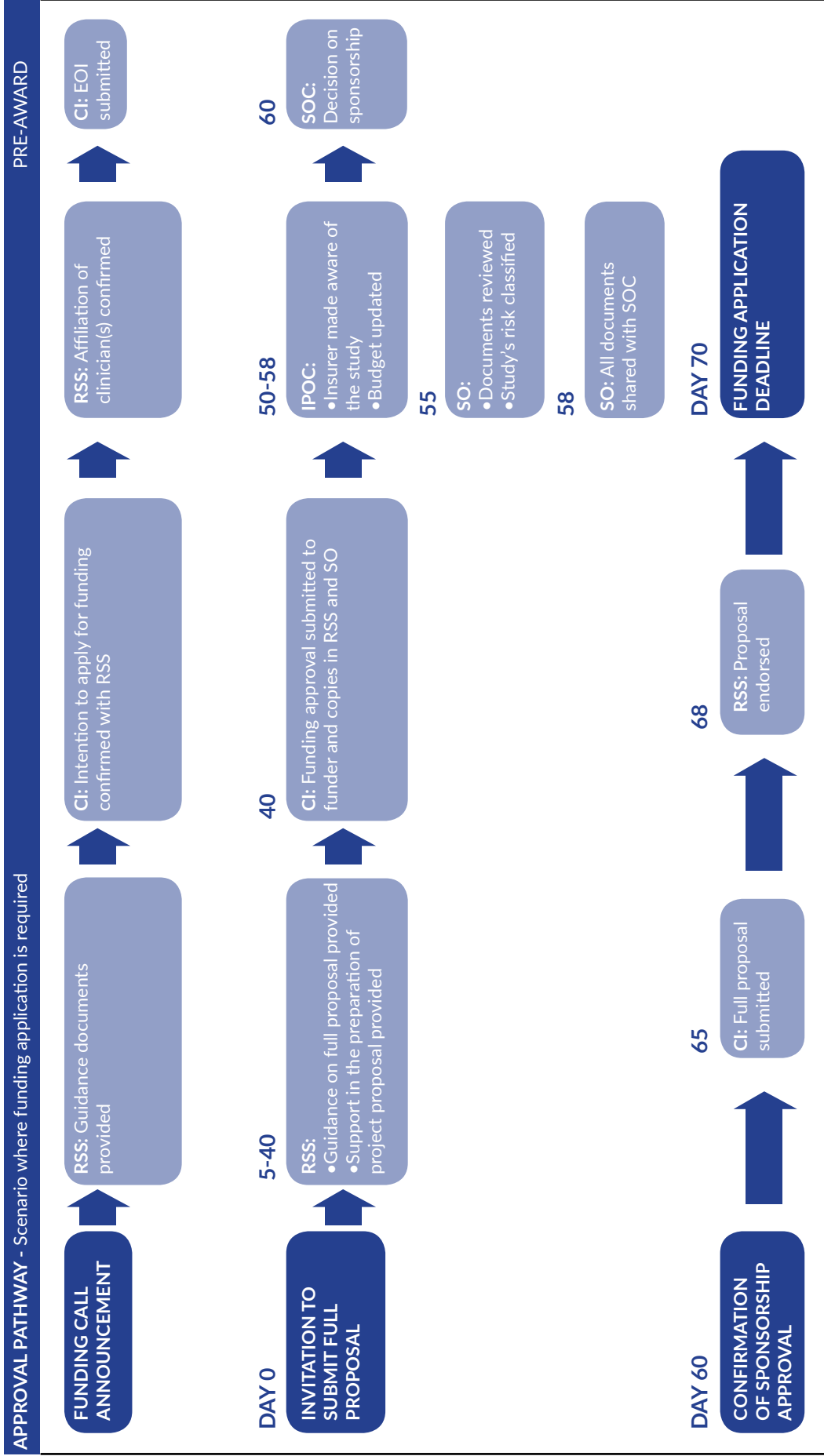
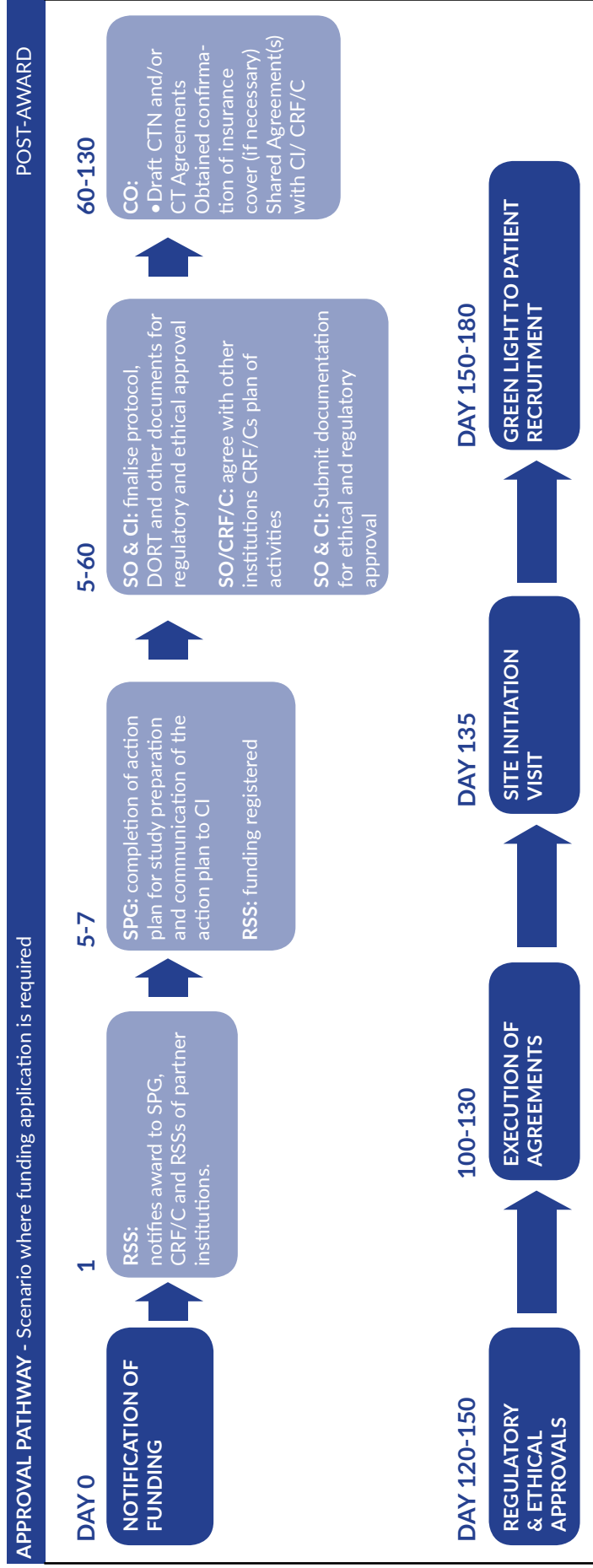


Diagram 4: Sample Approval Pathway – Post-Award



Abbreviations: RSS: Research Support Services CI: Chief Investigator SO: Sponsorship Officer SPG: Study Planning Group DORT: Division of Responsibilities
Table CRF/C: Clinical Research Facility/Centre CTN: Clinical Trial Network CTA: Clinical Trial Agreement CO: Contract Officer

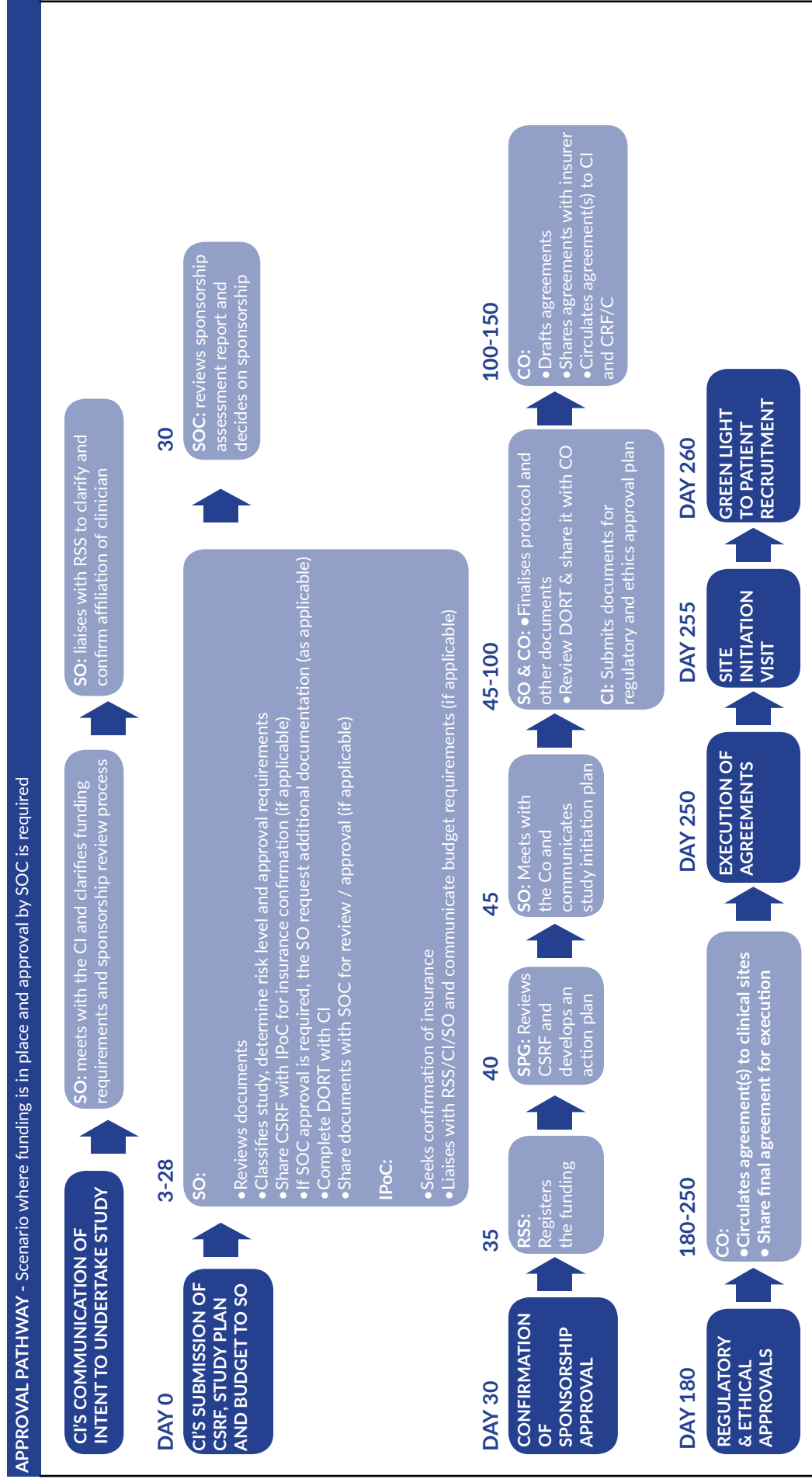
4b. Scenario where funding is in place and approval by the SOC is required

Table 6: Sample Approval Pathway – Where Funding Is in Place

Timeline (days)	Activity
0	Notification of Funding
	<p>Chief Investigator (CI): Communicate to SO intent to undertake study, which avails of funding support, and requires academic sponsorship.</p> <p>Sponsor Office(r) (SO): Meets with CI to clarify funding and sponsorship review process (and timelines), provides guidance and documentation for the preparation of sponsorship application (including, among others, budget template and CSRF, risk benefit analysis) and assess broadly the availability of funding to cover sponsorship and clinical research support costs. If it becomes apparent that the funding is not sufficient, the SO provides advice on what is the Institutional position on the support of studies with insufficient funding and provides guidance on the procedure to follow if there an opportunity to apply for institutional support.</p> <p>SO: Liaises with RSS to seek confirmation of affiliation of clinician with academic institution. If the CI has no affiliation (for example employment contract or honorary/adjunct appointment), the SO share with the CI the institutional guidance document on how (if possible) to apply for affiliation. The sponsorship approval process is put on hold until the confirmation of affiliation is in place.</p>
0	CI: Submit CSRF, study plan, and budget to SO.
3-28	<p>SO:</p> <ul style="list-style-type: none"> • Reviews study plan, the budget (to ensure that the study is sustainable), the CSRF and classifies the study's risk. • If the study falls under the low risk category, the SO issue letter of approval to proceed, subject to ethical approval. • If the study falls under the medium/high risk category, the SO completes with the CI the SRAF. • If the SRA identifies medium risk the Sponsor Office(r) issues letter of approval to proceed subject to ethical approval and site initiation visit. • If the SRA identifies high risk, the SO asks the CI to carry out a risk benefit analysis. In parallel the SO shares the CSRF with the IPoC for Insurance/indemnity confirmation. <p>SO, and CI: Completes division of responsibilities table.</p>
10-20	<p>IPoC:</p> <ul style="list-style-type: none"> • Sends CSRF to insurer to determine whether institutional policy would cover the study or additional premium applies. • Upon receipt of response from insurer, liaises with CI to update budget (if necessary) and with SO to clarify insurance/indemnity.
28	SO: Upon receipt of risk benefit analysis, confirmation of insurance/indemnity, confirmation of budget, submits SRA to Sponsorship Oversight Committee (SOC), including supporting documentation (confirmation of CI's affiliation, executive summary of the study plan and contributors, risk benefit analysis, confirmation of insurance/indemnity, budget, DORT).
30	SOC: Reviews sponsorship assessment report and decides on sponsorship (subject to ethics, and regulatory approvals).
30	Confirmation of sponsorship approval (subject to funding) – communication to PI and SPG.
32	SO: Organises SPG meeting.
35	RSS: Registers the funding.
40	<p>SPG:</p> <ul style="list-style-type: none"> • Reviews CSRF and identifies requirements to be met before the study can commence. • Develops an action plan for the study preparation based on requirements outlined in Annex 4.
45	SO: Meets with the CI, communicates/clarifies study initiation plan, offers support, if necessary.

Timeline (days)	Activity
45-100**	<p>SO, with CI:</p> <ul style="list-style-type: none"> • Review and finalise protocol and other documents required for ethical and regulatory approval. • Review DORT and share it with CO. <p>***Protocol development is dependent on study complexity and can generally take from 2– 6 months, up to 1 year (for more complex protocols). In these instances, the timelines in this table need to be adjusted.</p>
100	<p>CI: submits documents for regulatory and ethics approval</p>
100-150	<p>Contract Officer (CO):</p> <ul style="list-style-type: none"> • Drafts agreements. • If necessary, shares agreement with Insurer to confirm cover. • Circulates agreement(s) to CI and CRF for internal review and approval.
180	<p>Regulatory (& ethical) approval.</p>
180-250	<p>CO:</p> <ul style="list-style-type: none"> • Circulates agreement(s) to clinical sites, seeks feedback and makes amendments. • Share final agreement for execution.
250	<p>Execution of agreements.</p>
255	<p>SO: Site initiation visit.</p>
260	<p>Green light to patient recruitment.</p>

Diagram 5: Sample Approval Pathway – Scenario where funding is in place and approval by the SOC is required



Abbreviations: **RSS:** Research Support Services **CI:** Chief Investigator **SO:** Sponsorship Officer **CSRf:** Clinical Study Registration Form **SPG:** Study Planning Group **SOC:** Sponsorship Oversight Committee **IPoC:** Insurance Point of Contact **CO:** Contract Officer

Clinical Study Registration Form (CSRF)

This sample form serves as a first notification by a chief investigator to his/her academic institution of his/her plan to undertake a clinical research project. The completion of this form is required for any interventional or observational or epidemiological or physiological research study which involves humans, human tissue and/or data, regardless of the source of funding, use of investigational medicinal product (IMP) or device.

This form should be completed as early as possible and submitted to the academic institution's Sponsor Office(r) (SO) together with any other documentation available at that time (such as study protocol, patient information leaflet, investigators brochure, the risk/benefit analysis document). The SO will review the form and any documents provided with it to classify the study and its risk level as described in Table 3.

Depending on the risk level, the SO will determine whether confirmation of insurance/indemnity, sponsorship risk assessment and approval are required.

The SO may share the form (and any documentation associated with it) with the State Claims Agency (SCA) and/or the academic institution's underwriters.

Please ensure that the responses provided in the form are comprehensive, clear and can be understood by non-scientific or clinical personnel).

Clinical Study Registration Form

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 human subjects 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:**Clarify if the study requires HPRA approval and if so, whether it has been obtained as yet:**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/centre (CRF/C)?

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

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:

Please click the boxes as appropriate:

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:

Please click the boxes as appropriate:

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 Office(r) (SO)

SO's name:

Review date: XX/XX/XXX

Study's reference number:

Preliminary risk classification:

Low Medium High Very 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

Sponsorship Risk Assessment Form (SRAF)

Sponsorship Risk Assessment Form	
<ul style="list-style-type: none"> • <i>This form should be completed by the chief investigator (CI) and the Sponsor Office(r) (SO) (or nominee/equivalent).</i> • <i>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.</i> 	
CI's name:	
Title of proposed trial:	
Short title:	
Primary trial objective(s):	
Secondary trial objective(s):	
Trial Classification: Non-interventional - observational <input type="checkbox"/> Interventional - non-regulated <input type="checkbox"/> Interventional regulated <input type="checkbox"/>	
Trial Phase	
Trial Design and Complexity: (indicate all that apply) Open label <input type="checkbox"/> Placebo controlled <input type="checkbox"/> Randomised - indicate no of trial arms <input type="checkbox"/> Blinded <input type="checkbox"/> Cross over <input type="checkbox"/> Other - specify design (e.g. 2x2 factorial):	
Trial Participants: (indicate all that apply) Healthy volunteers <input type="checkbox"/> Patients <input type="checkbox"/> Patients with poor prognosis/terminal disease <input type="checkbox"/> Patients in emergency situations (e.g. unconscious) <input type="checkbox"/> Patients incapable of giving consent personally <input type="checkbox"/> Children under 5 years of age <input type="checkbox"/> Children between 5 -16 years of age <input type="checkbox"/> Women of childbearing potential (no contraception requirement in protocol) <input type="checkbox"/> Pregnant or nursing women <input type="checkbox"/> Other - specify:	
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 PPFV and LPLV timeline into consideration)			
Estimated Set-Out and Close Out Duration: (months)			
Total Duration of the Trial <ul style="list-style-type: none"> • 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 <input type="checkbox"/> Multiple <input type="checkbox"/> 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 <input type="checkbox"/> Medium <input type="checkbox"/> High <input type="checkbox"/> Very High <input type="checkbox"/> Mitigation Plan:			
How is the trial being funded? (Check more than one box if multiple sources of funding apply) Commercial source <input type="checkbox"/> Public or charity funded <input type="checkbox"/> In-house funds, specify the account details:			
Has funding already been secured for the trial? <input type="checkbox"/> Yes <input type="checkbox"/> 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 <input type="checkbox"/> No <input type="checkbox"/> If it is not sufficient, please clarify <i>(budget required for sponsorship approval)</i>			

Funding Risks Identified: Risk Level: Low <input type="checkbox"/> Medium <input type="checkbox"/> High <input type="checkbox"/> Very High <input type="checkbox"/> Mitigation Plan:
Training and experience Has the CI adequate GCP training? Yes <input type="checkbox"/> No <input type="checkbox"/> <i>If no, green light will be subject to confirmation of adequate GCP training</i> Has the chief investigator suitable experience? (a) in the therapeutic area of the proposed study? Yes <input type="checkbox"/> No <input type="checkbox"/> (b) in conducting the type of study that is proposed? Yes <input type="checkbox"/> No <input type="checkbox"/> (c) in use of the IMP (or trial procedures in the case of a surgical intervention)? Yes <input type="checkbox"/> No <input type="checkbox"/> 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 <input type="checkbox"/> No <input type="checkbox"/> Additional information:
Risks Identified: Risk Level: Low <input type="checkbox"/> Medium <input type="checkbox"/> High <input type="checkbox"/> Very High <input type="checkbox"/> Mitigation Plan:
For randomised trials only Have randomisation personnel/systems already been identified? No <input type="checkbox"/> Yes <input type="checkbox"/> If yes, please specify: Is it already known who will assign the treatment allocations? No <input type="checkbox"/> Yes <input type="checkbox"/> If yes, please specify: Is the treatment blinded? No <input type="checkbox"/> Yes <input type="checkbox"/> If yes, please specify:
Risks Identified: Risk Level: Low <input type="checkbox"/> Medium <input type="checkbox"/> High <input type="checkbox"/> Very High <input type="checkbox"/> Mitigation Plan:
Information about the IMP Product name: Dose:

Name of active substance:Pharmaceutical Form: Tablet / Capsule Powder for Reconstitution

Other – 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 rationale

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 rationale

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 rationale

How will the IMP be stored?as per SmPC Other, please provide further details and rationale **Risks Identified:**Risk Level: Low Medium High Very 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 Very 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 Very 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 Very 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? <i>*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.</i>			
Does the CI have any other conflict interests* in the company/manufacturer supplying the IMP/device or funding the trial? <i>*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.</i>			
Does the CI have any other conflict interests* in the company/manufacturer supplying the IMP/device or funding the trial? <i>*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.</i>			
Does the CI have any other conflict of interests?			
If the answer is yes to any of the questions above, please provide details:			
<p>Is the CI currently under investigation for misconduct, or for any other reason? Yes <input type="checkbox"/> No <input type="checkbox"/> If yes above, please details:</p>			
<p>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 <input type="checkbox"/> No <input type="checkbox"/> If yes above, please details:</p>			

Risk Level: <input type="checkbox"/> Low <input type="checkbox"/> Medium <input type="checkbox"/> High <input type="checkbox"/> Very 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 <input type="checkbox"/> No <input type="checkbox"/> 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 <input type="checkbox"/> No <input type="checkbox"/>	
Research Ethics approval Granted <input type="checkbox"/> Pending (the approval to proceed with the study is subject to ethics approval) <input type="checkbox"/>	
Regulatory approval Not applicable Granted <input type="checkbox"/> Pending (the approval to proceed with the study is subject to regulatory approval)	
Sponsor oversight role Ensure GCP compliance <input type="checkbox"/> Carry out site initiation visit and monitoring <input type="checkbox"/> Carry out site initiation visit only <input type="checkbox"/> No oversight <input type="checkbox"/>	

Division of Responsibilities Table Medicinal Products (DORT MP)

Note 1: Parties should set out the agreed division and/or delegation of responsibilities in the table below. Some responsibilities are only applicable to particular types of study. Any additional responsibilities to those set out in this table should be added at the end to preserve the numbering of the standard list and navigation of the contents.

Note 2: All references to subjects refer to those recruited at or through the site.

S: Sponsor

3rd: 3rd party vendors

C: comments

CI: chief investigator

H: hospital

Responsibility	Responsible Party				
	S	CI	3rd	H	C
1. STUDY PLANNING AND PREPARATORY ACTIVITIES					
Study Preparation and Application for Sponsorship					
Protocol development					
Develop study plan					
Complete study insurance and registration form and submit to sponsorship office					
Review CRSF and complete sponsor risk assessment if required					
Develop a risk mitigation plan					
Sponsorship oversight committee review of application					
Undertake medical review of the protocol and benefit/risk analysis					
Write grant/funding application (if applicable)					
Coordinate grant application support and review - endorse application					
Ensure that the protocol undergoes scientific review					
Ensure that the protocol is in compliance with the relevant regulations/guidelines					
Prepare patient information leaflet and consent form, including where appropriate consent to providing subject tissue, sample, medical data or other material and other relevant documents prior to ethics submission					
Confirm sponsorship support (in full or in principle)					
Study Set Up and Documentation					
Develop a data management plan					
Design and prepare Case Report Forms (CRFs)					
Approve CRFs					
Develop the study database (eCRF)					
Develop eCRF completion guidelines					
Develop the randomisation system and emergency unblinding procedures					
Complete computer system validation on the study database(s)					
Establish the trial master file (TMF)					
Establish the investigator site file(s) (ISFs)					
Establish study management/oversight committee(s), advisory group(s) and charters					
Site selection					
Site feasibility					

Responsibility	Responsible Party				
	S	CI	3rd	H	C
Site initiation					
Obtain EudraCT number/EUDAMED ID					
Register the trial in applicable registries					
Develop study specific procedures					
Prepare patient information leaflet and consent form					
Develop the laboratory manual					
Develop a study communication plan					
Statistical analysis plan (SAP) development					
Develop a study monitoring plan					
Identify the reference safety information					
Establish the IMP dossier					
Establish IMP/device recall procedure					
Costing, Funding and Procurement					
Develop study budget					
Seek quotes for product(s) and service(s)					
Budget negotiation with site(s)					
Secure and administer funding					
Distribute funding to clinical sites according to payment schedules					
Ensure that funding is spent according to funder terms and conditions (if applicable)					
Data Protection					
Complete data protection impact assessment and put in place management plan that meets the data controller(s) requirements					
Review data protection impact assessment and management plan on an ongoing basis					
Insurance/Indemnity					
Ensure that clinical trial indemnity is in place (to cover study subject participation in the study)					
Confirm provision of malpractice /medical negligence indemnity					
Confirm employer and public liability cover for staff involved in the study who are employed by the academic institution					
Staffing – Competence, Guidance, Notification and Training					
Ensure that the clinical site team members are appropriately qualified, and experienced to undertake the conduct of the study					
Ensure that the clinical site team members have current substantive or honorary employment contracts in place, where required.					
Identify the study medical expert					
Assign tasks to the study team					
2. APPROVALS					
Clinical trial application to the ethics committee					
Clinical trial application to the competent authority					
Obtain clinical site(s) approval					
3. CONTRACTS					
Review, negotiate (if necessary), execute funding agreement					
Comply with funding terms and conditions					

Responsibility	Responsible Party				
	S	CI	3rd	H	C
Draft and negotiate collaboration and clinical trial agreements and ensure that they are executed timely, prior to green light					
Execute clinical trial agreement					
Ensure that service/material supply contracts are executed					
Execute service and material supply contracts					
Review and execute service contracts/third party contracts					
Put in place an investigator source data agreement					
4. PRE-GREEN LIGHT REQUIREMENTS					
Ensuring that any hospital's requirements are met in advance of clinical study start					
Complete regulatory green-light process					
Ensure that contracts have been signed prior to green light					
Confirmation of insurance cover					
5. POST-GREEN LIGHT STUDY IMPLEMENTATION AND OVERSIGHT					
Materials/Devices (investigational medicinal products (IMPs) or/and devices and/or laboratory materials)					
Ensure that IMP/materials/devices are supplied to the site					
Ensure that IMP/materials/devices are available to trial subjects in a sufficient amount and free of charge					
Ensure that IMP/materials/devices are handled and labelled stored in accordance with regulatory requirements and the protocol					
Maintain accountability records					
Ensure that IMP/materials/devices are not used for any purposes other than the conduct of the study					
QP release of IMP					
IMP manufacturers/importers authorisations in place					
Labelling of IMP/materials/devices					
Study conduct					
Ensure that the rights of individual subjects are protected, they have provided informed consent, receive appropriate medical care whilst participating in the study, including in the case of adverse events caused by the study IMP and/or device					
Inform appropriate health care professionals if their patient become a subject in the study					
Ensure facilities, resources and support at the clinical sites are adequate throughout the duration of the study					
Ensure that patient data protection rights are protected in accordance with GDPR					
Ensure that legislation in relation to research is followed within the clinical site					
Maintain and store safely investigator site file					
Execute the study in accordance with the protocol, GCP and the study approval					
Ongoing risk/benefit analysis					
Implement urgent safety measures					

Responsibility	Responsible Party				
	S	CI	3rd	H	C
Provide reports as agreed in the clinical trial protocol and agreements/contracts					
Submit annual progress reports to the ethic committee					
Report suspected research misconduct to the Sponsor					
Organise study meetings					
Review patient eligibility queries					
Patient registration					
Manage essential documents					
Monitor recruitment and withdrawals					
Make archiving arrangements					
Process biological samples					
Store biological samples					
Ship biological samples					
Analyse biological samples					
Pharmaco/Device Vigilance					
Report Serious Adverse Events (SAEs) to the sponsor according to the protocol					
Ensure that all SAEs that require immediate reporting are reviewed and assessed					
Ensure that all Suspected Unexpected Serious Adverse Reactions (SUSAR), are identified and fully reported to the Competent Authority and the relevant ethics committee(s) within the required timeframe					
Ensure that all investigators are aware of SUSARs occurring in relation to the IMP					
Promptly inform the competent authority, ethics committee(s) and investigators of any urgent safety measures taken to protect participants in the study					
Submit annual safety reports to the relevant authorities					
Ensure that annual safety reports are submitted to the competent authority and ethics committee within the required timeframes and copies sent to SOC (and DSC, if applicable)					
Annual review of RSI					
Review and process SAE reports					
Report SUSARs to Eudravigilance					
Manage data safety and monitoring board meetings					
Audits and Monitoring					
Ensure that all data and documentation are available for the purposes of inspections or audits					
Implement study monitoring plan					
Monitor the study for GCP and protocol compliance					
Perform medical monitoring, including benefit risk assessment					
Perform medical safety review of each safety report					
Commission independent audits					
Review and approve monitoring and audit reports					

Responsibility	Responsible Party				
	S	CI	3rd	H	C
Correction of any GCP, clinical trial protocol or study approval non-compliances identified during monitoring and independent audit reports					
Data Management					
Data entry					
Data monitoring					
Quality control of data					
Data cleaning					
Data analysis					
Ensure that data is managed and analysed as planned					
Provide reports to SOC (and DSC, if applicable)					
Ensure appropriate archiving of statistics documentation, data set and programming for the trial					
Investigational Medicinal Product Management					
IMP planning					
Approval of IMP release to sites					
Monitor IMP levels across sites					
Manage IMP at site					
Destruction of IMP					
Protocol Amendments					
Prepare protocol amendments					
Seek approval for substantial protocol amendments from the SO/SOC, the ethics committee, the competent authority and the clinical site.					
Review and sign of protocol amendments					
Ensure investigators are aware of dates of amendment approval, for implementation and appropriate completion of training					
6. END OF STUDY					
Site Close Out					
Resolve all open queries at sites					
Final IMP/device accountability					
Arrange IMP/device destruction					
Conduct close-out visits					
Review and approve close-out visit reports					
Data Management and Statistical Analysis					
Database cleaning and reconciliation in preparation for database lock					
Database lock					
Statistical analysis					
Notification and Reporting					
Notify the competent authority(ies), relevant ethics committee and site(s) if the study is terminated early.					
Notify the competent authority (ies), relevant ethics committee and site(s) of the end of the study.					
Ensure that final safety report is generated and submitted to the competent authority and ethics committee					

Responsibility	Responsible Party				
	S	CI	3rd	H	C
Preparation and approval clinical study report					
Submit clinical study report to the ethics committee and competent authority					
Update EudraCT and relevant registries with end of trial information					
Archiving					
Archive the trial master file					
Archive the ISF(s)					
Archive the trial database					
Dissemination					
Agree authors list and publication plan					
Manuscript/poster development					
Submission of manuscript for publication or poster presentation					
Others					

Division of Responsibilities Table Medical Devices (DORT MD)

Note 1: Parties should set out the agreed division and/or delegation of responsibilities in the table below. Some responsibilities are only applicable to particular types of study. Any additional responsibilities to those set out in this table should be added at the end to preserve the numbering of the standard list and navigation of the contents.

Note 2: All references to subjects refer to those recruited at or through the site.

S: Sponsor

3rd: 3rd party vendors

C: comments

CI: chief investigator

H: hospital

Responsibility	Responsible Party				
	S	CI	3rd	H	C
1. INVESTIGATION PLANNING AND PREPARATORY ACTIVITIES					
Investigation Preparation and Application for Sponsorship					
Develop overall device investigation plan					
Clinical Investigation Plan (CIP) development					
Complete clinical study insurance and registration form and submit to sponsorship office					
Review form and complete sponsor risk assessment					
Perform a risk assessment of the clinical procedure and share with interested parties					
Conduct an on-site audit of the manufacturing facility					
Obtain an independent risk assessment of the device (if required) and share with interested parties					
Develop a risk mitigation plan					
Sponsorship oversight committee review of application					
Undertake medical review of the clinical investigation plan and benefit/risk analysis					
Write grant/funding application (if applicable)					
Coordinate grant application support and review - endorse application					
Ensure that the CIP undergoes scientific review					
Ensure that the CIP is in compliance with the relevant regulations/guidelines					
Prepare patient information leaflet and consent form, including where appropriate consent to providing subject tissue, sample, medical data or other material and other relevant documents prior to ethics submission					
Confirm sponsorship support (in full or in principle)					
Investigation Set Up and Documentation					
Develop a data management plan					
Design and prepare Case Report Forms (CRFs or eCRFs)					
Approve CRFs					
Develop the investigation database					
Develop eCRF completion guidelines/instructions					
Develop the randomisation system and emergency unblinding procedures					

Responsibility	Responsible Party				
	S	CI	3rd	H	C
Complete computer system validation on the investigation database(s)					
Establish the trial master file (TMF)					
Establish the investigator site file(s) (ISFs)					
Establish investigation management/oversight committee(s), advisory group(s) and charters					
Site selection					
Site feasibility					
QMS certification of clinical site (JCI certificate)					
Site Initiation					
Register the investigation in applicable registries (EUDAMED)					
Develop investigation specific procedures					
Prepare patient information leaflet and consent form					
Develop the laboratory manual					
Develop an investigation communication plan					
Statistical analysis plan (SAP) development					
Develop an investigation monitoring plan					
Costing, Funding and Procurement					
Develop investigation budget					
Seek quotes for product(s) and service(s)					
Budget negotiation with site(s)					
Secure and administer funding					
Distribute funding to clinical sites according to payment schedules					
Ensure that funding is spent according to funder terms and conditions (if applicable)					
Data Protection					
Complete data protection impact assessment and put in place management plan that meets the data controller(s) requirements					
Review data protection impact assessment and management plan on an ongoing basis					
Insurance/Indemnity					
Ensure that clinical investigation indemnity is in place (to cover subject participation in the investigation)					
Confirm provision of malpractice/medical negligence indemnity					
Confirm employer and public liability cover for staff involved in the investigation who are employed by the academic institution					
Staffing – Competence, Guidance, Notification and Training					
Ensure that the clinical site team members are appropriately qualified, and experienced to undertake the conduct of the investigation					
Ensure that the clinical site team members have current substantive or honorary employment contracts in place, where required.					
Identify the investigation medical expert					
Assign tasks to the investigation team					

Responsibility	Responsible Party				
	S	CI	3rd	H	C
2. APPROVALS					
Clinical investigation application to the ethics committee					
Clinical investigation application to the competent authority for letter of no objection					
Obtain clinical site(s) approval					
3. CONTRACTS					
Review, negotiate (if necessary), execute funding agreement					
Comply with funding terms and conditions					
Draft and negotiate collaboration and clinical investigation agreements and ensure that they are executed in a timely manner, prior to green light					
Execute clinical investigation agreement					
Ensure that service/material/investigational medical device supply contracts are executed					
Execute service/material/investigational medical device supply contracts					
Review and execute service contracts/third party contracts					
Put in place an investigator source data agreement					
4. PRE-GREEN LIGHT REQUIREMENTS					
Ensuring that any hospital requirements are met in advance of clinical investigation start					
Complete regulatory green-light process					
Ensure that contracts have been signed prior to green light					
Confirmation of insurance cover					
5. POST-GREEN LIGHT INVESTIGATION IMPLEMENTATION AND OVERSIGHT					
Devices/Materials (devices and/or laboratory materials)					
Manufacture, quality control and quality assurance batch release of investigational medical device					
QMS Certificate for manufacturing site					
Investigational medical device product release certificate					
Ensure that investigational medical devices are supplied to the site					
Ensure that investigational medical devices are available to investigation subjects in a sufficient amount and free of charge					
Ensure that investigational medical devices are handled and labelled stored in accordance with regulatory requirements and the CIP					
Ensure that investigational medical devices are not used for any purposes other than the conduct of the investigation					
Labelling of materials/devices					
Maintain accountability records					
Establish device recall procedure					
Ensure device specification and device instructions for use are in place and available to investigator					
Ensure any other materials or medicinal products required during the investigation (including rescue medication) are available					

Responsibility	Responsible Party				
	S	CI	3rd	H	C
Investigation Conduct					
Ensure that the rights of individual subjects are protected, they have provided informed consent, receive appropriate medical care whilst participating in the investigation, including in the case of adverse events					
Inform appropriate health care professionals if their patient become a subject in the investigation					
Ensure facilities, resources and support at the clinical sites are adequate throughout the duration of the investigation					
Ensure that patient data protection rights are protected in accordance with GDPR					
Ensure that legislation in relation to research is followed within the clinical site					
Maintain and store safely investigator site file					
Execute the investigation in accordance with the CIP, GCP and the approvals					
Ongoing risk/benefit analysis					
Implement urgent safety measures					
Provide reports as agreed in the CIP and agreements/contracts					
Submit annual progress reports to the EC					
Report suspected research misconduct to the Sponsor					
Organise investigation meetings					
Review patient eligibility queries					
Patient registration					
Manage essential documents					
Monitor recruitment and withdrawals					
Make archiving arrangements					
Process biological samples					
Store biological samples					
Ship biological samples					
Analyse biological samples					
Device Vigilance					
Report serious adverse events (SAEs) to the sponsor according to the CIP					
Ensure that all SAEs that require immediate reporting are reviewed and assessed					
Ensure that all reportable SAEs (as detailed in the CIP), are identified and fully reported to the competent authority and the relevant ethics committee(s) within the required timeframe					
Ensure that all reportable device deficiencies (as detailed in the CIP), are identified and fully reported to the competent authority and the relevant ethics committee(s) within the required timeframe					
Promptly inform the competent authority, ethics committee(s) and investigators of any urgent safety measures taken to protect participants in the investigation					

Responsibility	Responsible Party				
	S	CI	3rd	H	C
Notify notified body or competent authority of any non-conformances relating to manufacture, testing, supply or storage of investigational medical device					
Submit annual safety reports to the relevant authorities					
Ensure that annual safety reports are submitted to the competent authority and ethics committee within the required timeframes and copies sent to SOC (and DSC, if applicable)					
Annual review of device specifications and instructions for use					
Review and process SAE reports and device deficiency reports					
Manage data safety and monitoring board meetings					
Audits and Monitoring					
Ensure that all data and documentation are available for the purposes of inspections or audits					
Implement Investigation monitoring plan					
Monitor the investigation for GCP and CIP compliance					
Perform medical monitoring, including benefit risk assessment					
Perform medical safety review of each safety report					
Commission independent audits					
Review and approve monitoring and audit reports					
Correction of any GCP, CIP or investigation approval non-compliances identified during monitoring and independent audit reports					
Data Management					
Data entry					
Data monitoring					
Quality control of data					
Data cleaning					
Data analysis					
Ensure that data is managed and analysed as planned					
Provide reports to SOC (and DSC, if applicable)					
Ensure appropriate archiving of statistics documentation, data set and programming for the investigation					
Investigational Medical Device (IMD) Management					
IMD planning					
Approval of IMD release to sites					
Monitor IMD levels across sites					
Manage IMDs at site					
Destruction of IMDs					
Clinical Investigation Plan (CIP) Amendments					
Prepare CIP amendments					
Seek approval for substantial CIP amendments from the SO/SOC, the ethics committee, the competent authority and the clinical site.					
Review and sign of CIP amendments					
Ensure investigators are aware of dates of amendment approval, for implementation and appr					

Responsibility	Responsible Party				
	S	CI	3rd	H	C
6. END OF INVESTIGATION					
Site Close Out					
Resolve all open queries at sites					
Final IMD accountability					
Arrange IMD destruction					
Conduct close-out visits					
Review and approve close-out visit reports					
Data Management and Statistical Analysis					
Database cleaning and reconciliation in preparation for database lock					
Database lock					
Statistical analysis					
Notification and Reporting					
Notify the competent authority (ies), relevant ethics committee and site(s) if the investigation is terminated early.					
Notify the competent authority (ies), relevant ethics committee and site(s) of the end of the investigation.					
Ensure that final clinical investigation report is generated and submitted to the competent authority and ethics committee					
Preparation and approval clinical investigation report					
Submit clinical investigation report to the ethics committee and competent authority					
Update any relevant registries (EUDAMED) with end of investigation information					
Archiving					
Archive the trial master file					
Archive the ISF(s)					
Archive the investigation database					
Dissemination					
Agree authors list and publication plan					
Manuscript/poster development					
Submission of manuscript for publication or poster presentation					
Others					

Annex 4: Sponsor Oversight Committee Report (SOCR)

The following documentation must be submitted in advance by the Sponsor Officer (SO) to the Sponsorship Oversight Committee (SOC):

- All available study supporting documentation (such as protocol or grant application, budget proposal, confirmation of insurance/indemnity)
- Clinical study registration form
- Completed sponsorship risk assessment form
- Data protection impact assessment and management plan
- Risk/benefit analysis document (no template applicable)
- Risk assessment according to ICH-GCP methodology (for high risk studies only)
- Division of responsibilities table

This section is completed following a review of the above documentation supporting the project proposal by the Sponsor Oversight Committee. Completion of this section and the signature below documents the decision of the SOC.

SPONSOR OVERSIGHT COMMITTEE REPORT		
SOC Meeting Date (DD/MMM/YYYY)		
Have the risk mitigation activities listed in the SRAF to an acceptable level? Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>		
If 'No' provide details: <div style="border: 1px solid black; height: 40px; width: 100%;"></div>		
Sponsorship Decision: Tick as appropriate a) Sponsorship approval granted* <input type="checkbox"/> b) Sponsorship decision 'on-hold' pending additional clarification/risk mitigation <input type="checkbox"/> c) Sponsorship denied <input type="checkbox"/> *Sponsorship approval at this point is granted subject to the following conditions/requirements being met (if not available): Confirmation of funding <input type="checkbox"/> Confirmation of Insurance/indemnity <input type="checkbox"/> Ethics committee approval <input type="checkbox"/> Regulatory approval <input type="checkbox"/> Plan for risk mitigation activities and procedural requirements being fulfilled <input type="checkbox"/> Study green light <input type="checkbox"/> GCP training being undertaken by the study team <input type="checkbox"/>		
If 'B' or 'C' are ticked, please outline in detail the rationale for that decision and/ or clarify any additional detail required. <div style="border: 1px solid black; height: 100px; width: 100%;"></div>		
SOC representative signature: <div style="border: 1px solid black; height: 40px; width: 100%;"></div>		
----- Print name	----- Sign	----- Date

Classification Based Post Approval Requirements Tables

Table 7: NON-INTERVENTIONAL STUDIES

TYPE	OBSERVATIONAL	BIOBANKING	DATA
Guidance	ICH GCP & Declaration of Helsinki		
Legislation applicable	Data protection directive -> GDPR		
Ethical approval requirements	Local REC		
Regulatory authority oversight	No regulatory oversight for conduct of clinical study – data protection commissioner > independent supervisory authority for the processing of personal data		
Insurance/indemnity requirements	Refer to SIG document - https://stateclaims.ie/resources		
Other requirements			
Statistical analysis	YES		
Reporting to Sponsor oversight committee	NO		
Monitoring	YES (for data management) Monitoring not required unless concerns regarding inexperienced research staff, history of data breach, history of concerns regarding informed consenting process.		
Quality management requirements			
SOPs	YES		
Record management system	YES		
Internal Audits	Yes (for data protection)		
Subject to audits	NO for study - YES for data protection		

Table 8: INTERVENTIONAL STUDIES ON IMPs (excluding devices)

TYPE	REGULATED	NON-REGULATED
Guidance	ICH GCP & Declaration of Helsinki	
Legislation applicable	CT directive SI 190/2004 (requires ICH GCP compliance) Data protection directive -> GDPR	ICH GCP compliance Data protection directive -> GDPR
Ethical approval requirements	National REC	Local REC
Regulatory authority oversight and approval requirements	For the study: HPRA approval required For personal data: Independent Supervisory Authority (no approval required)	
Requirement for external expertise	To be assessed on a case by case basis	
Insurance/indemnity requirements	Refer to SIG document - https://stateclaims.ie/resources	
Other requirements		
Project Management Plan, including:	YES	YES, for high risk only
Plan for notification and management of adverse events or device events	YES	YES, for high risk only
Monitoring plan	YES - frequency dependent on risk	YES, for high risk only - frequency dependent on risk
Pharmacovigilance Plan	YES	YES, for high risk regulated only
Plan for reporting to Sponsor oversight committee (e.g. DSMC)	To agree requirements and when applicable	
Statistical analysis	YES	
Quality management requirements		
SOPs	YES	
Record management system	YES	
Internal audit	YES	Advisable

Table 9: INTERVENTIONAL STUDIES ON DEVICES

TYPE	REGULATED		NON-REGULATED	
	CE Marked & Non CE Marked		CE Marked	Non CE Marked
Guidance	ISO 14155, ISO 14971, ISO 13485, ISO 31000, IEC 62304, IEC 62366; Declaration of Helsinki			
Legislation applicable	Medical Device Directives: Directive 90/385/EEC regarding active implantable medical devices (AIMD); Directive 93/42/EEC regarding medical devices (MDD); Directive 98/79/EC regarding in vitro diagnostic medical devices (IVDD); Medical Device Regulation (EU) 2017-745 (regarding medical devices and active implantable medical devices); In Vitro Diagnostic Medical Devices Regulation (EU) 2017/746; ISO 13485, ISO 14155, ISO 14971; EU General Data Protection Regulation (GDPR)			
Ethical approval requirements	Local REC			
Regulatory Authority oversight and approval requirements	For studies with commercial intent HPRAs approval and oversight applies For personal data: Independent Supervisory Authority (no approval required)		For studies with no commercial intent HPRAs approval and oversight do not apply (seek confirmation that HPRAs approval and oversight are not required) For personal data: Independent Supervisory Authority - no approval required	
Requirement for external expertise	No		YES - Low Touch: in risk documentation and clinical evaluation documentation review to confirm that there is no unanticipated risk associated with off-label use of the CE Marked device.	YES - High Touch: in regulatory requirements and manufacturing quality system for medical devices (consideration should be given to cost and time implications if commitment to sponsorship is required at grant application stage)
Where Sponsor role rests (subject to approval)	Academic Institution or manufacturer			
Other requirements				
Project Management Plan including	YES		YES (high risk only)	
Sponsored Manufacturing Audit Site	NO			YES (high risk only)
Monitoring plan	YES - frequency dependent on risk		YES - (high risk only) frequency dependent on risk	
Pharmacovigilance Plan	NO (unless the device implies administration of drug)			

TYPE	REGULATED		NON-REGULATED	
	CE Marked & Non CE Marked		CE Marked	Non CE Marked
Device Safety Plan	YES		YES (high risk only)	
Plan for reporting to Sponsor oversight committee (e.g. DSMC)	To agree requirements and when applicable			
Statistical Analysis	YES			
Quality management requirements				
SOPs	YES			
Record management system	YES			
Other	Certification of manufacturing quality management system			
Internal audit/ Self Inspection	YES			
Subject to HPRA audits	YES		N/A	
Insurance/ indemnity requirements	Refer to SIG document - https://stateclaims.ie/resources			

ISO 14155 details the requirements for the conduct of clinical investigation of medical devices – it outlines good clinical practice for investigations of medical devices

Notified Body: A notified body is an organisation designated by an EU country to assess the conformity of certain products before being placed on the market. These bodies carry out tasks related to conformity assessment procedures set out in the applicable legislation, when a third party is required. The European Commission publishes a list of such notified bodies. Medical Device manufacturers choose their Notified Body and provide evidence of compliance to the applicable directives and regulations regarding their device in order to receive CE Marking of the product.

ISO 14971 defines risk management requirements for medical device product design & development, manufacturing and use. This standard specifies a process for a manufacturer to identify the hazards associated with medical devices, including in vitro diagnostic (IVD) medical devices, to estimate and evaluate the associated risks, to control these risks, and to monitor the effectiveness of the controls. The requirements of ISO 14971:2012 are applicable to all stages of the life cycle of a medical device.

ISO 31000 defines risks affecting organisations can have consequences in terms of economic performance and professional reputation, as well as environmental, safety and societal outcomes.

IEC 62304 defines the life cycle requirements for medical device software. The set of processes, activities, and tasks described in this standard establishes a common framework for medical device software life cycle processes.

IEC 62366 specifies a process for a manufacturer to analyse, specify, design, verify and validate usability, as it relates to safety of a medical device. This usability engineering process assesses and mitigates risks caused by usability problems associated with correct use and use errors, i.e. normal use. It can be used to identify but does not assess or mitigate risks associated with abnormal use.

Contractual Framework for Data Protection

The Contract and Legal WG worked with an external legal firm to develop a contractual framework which address the contractual requirement of Article 28 of General Data Protection Regulation (GDPR) in clinical trials.

The contractual framework, which is reflected in the template clinical trial agreement (CTA) available at the following link - www.crdi.ie/corporate-enabling-of-clinical-research - is based on the following definitions, roles and responsibilities:

Clinical Trial Data/Documentation – this is data generated about study subjects as a direct result of the clinical trial that would not otherwise have been generated. It is collected by hospital's or academic institution's employees and then uploaded on to the sponsor's eCRF/ electronic system. The academic Sponsor is the data controller of the trial data/clinical trial documentation, whereas the hospital site (who employs the trial site team) and any other entity (who employ trial site team members) are “data processor” (see Annex A) in respect of this data.

To comply with Article 28 of GDPR, the WG recommend that CTA include the data processing provisions with respect of clinical trial data/documentation, in accordance with the CECR model CTA.

Medical Records – they are records kept by the hospital in relation to the treatment of a study subject, excluding trial data/study documentation. The hospital is a data controller of medical records for the purpose of delivering clinical care.

Subject to patient consent, it is often necessary for the clinical trial Sponsor to access medical records for the purpose of research.

In this instance, the Sponsor and the clinical site have separate controller roles for medical records as they have set distinct purposes, for example delivery of care (purpose set by the clinical site) and clinical research (purpose set by the Sponsor of the clinical trial).

While it is not a regulatory requirement, with the advent of GDPR it is considered good practice to include contractual clauses in the CTA clarifying separate controllers' arrangements, so the parties are clear on their role and responsibilities.

It is therefore recommended that the CTA includes “data sharing” provisions that clarify the separate controllers' roles and responsibilities with respect to medical records, in accordance with the CECR model CTA.

To comply with Article 28 of GDPR, data processing provisions will also apply to any institution (other than the Sponsor and the hospital which controls the medical records) whose employees process medical records for the purpose of the clinical trial.

It is therefore recommended that in this instance the data processing provisions included in the CECR model CTA are used for governing also the processing of medical records.

A joint controller role may apply in instances where two or more institutions have jointly/ collaboratively defined the purpose of the research.

Potential Role(s) (for purposes of GDPR)

Data Controller	Data Processor	Separate Data Controllers / Data Controller-in-Common	Joint Data Controller
<p>Article 4 of GDPR⁹ defines data controllers as:</p> <p>(7) ‘controller’ means the natural or legal person, public authority, agency or other body which, alone or jointly with others, determines the purposes and means of the processing of personal data; where the purposes and means of such processing are determined by Union or Member State law, the controller or the specific criteria for its nomination may be provided for by Union or Member State law;</p> <p>So, in short, this person –</p> <ul style="list-style-type: none"> • who decides what personal data is going to be kept? • who decides the use to which the personal data will be put? <p>It is possible for one organisation or person to be both a data controller and a data processor, in respect of distinct sets of personal data. For example, a payroll company would be the data controller in respect of the data about its own staff, but would be the data processor in respect of the staff payroll data it is processing for its client companies</p> <p>For further info see the Irish Data Protection Commissioners Guidance Note¹⁰</p>	<p>Article 4 of GDPR¹¹ defines data controllers as:</p> <p>(8) ‘processor’ means a natural or legal person, public authority, agency or other body which processes personal data on behalf of the controller;</p> <p>So, in short, some other organisation decides and is responsible for what happens to the personal data</p> <p>For further info see the Irish Data Protection Commissioners Guidance Note¹²</p>	<p>GDPR does not expressly refer to processing of data by a controller “in common” with others.</p> <p>However, the Article 29 Data Protection Working Party Opinion 1/2010¹³ recognises that there may be situations when there is more than one data controller in respect of the same dataset</p> <p>As such, there is a view there is a distinction between what is a joint controller and a controller in common – in that:</p> <p>(a) joint controllers would be acting together to decide the purposes and manner data processing of the same pool of data;</p> <p>(b) whereas the data controllers in common share a pool of personal data that they process independently of each other.</p>	<p>Article 26 of GDPR¹⁴ defines joint data controllers as:</p> <p>(1) Where two or more controllers jointly determine the purposes and means of processing, they shall be joint controllers. They shall in a transparent manner determine their respective responsibilities for compliance with the obligations under this Regulation, in particular as regards the exercising of the rights of the data subject and their respective duties to provide the information referred to in Articles 13 and 14, by means of an arrangement between them unless, and in so far as, the respective responsibilities of the controllers are determined by Union or Member State law to which the controllers are subject. The arrangement may designate a contact point for data subjects.</p> <p>(2) The arrangement referred to in paragraph 1 shall duly reflect the respective roles and relationships of the joint controllers vis-à-vis the data subjects. The essence of the arrangement shall be made available to the data subject.</p> <p>(3) Irrespective of the terms of the arrangement referred to in paragraph 1, the data subject may exercise his or her rights under this Regulation in respect of and against each of the controllers.</p>

⁹ **Article 4 EU GDPR “Definitions”**, EU General Data Protection Regulation <http://www.privacy-regulation.eu/en/article-4-definitions-GDPR.htm>

¹⁰ **A Practical Guide to Data Controller**, Data Protection <https://www.dataprotection.ie/docs/Are-you-a-Data-Controller/y/43.htm>

¹¹ **Article 4 EU GDPR “Definitions”**, EU General Data Protection Regulation <http://www.privacy-regulation.eu/en/article-4-definitions-GDPR.htm>

¹² **A Practical Guide to Data Controller**, Data Protection <https://www.dataprotection.ie/docs/Are-you-a-Data-Controller/y/43.htm>

¹³ **Opinion 1/2010 on the concepts of “controller” and “processor”**, EU Commission https://ec.europa.eu/justice/article-29/documentation/opinion-recommendation/files/2010/wp169_en.pdf

¹⁴ **Article 26 EU GDPR “Joint Controllers”**, EU General Data Protection Regulation <http://www.privacy-regulation.eu/en/article-26-joint-controllers-GDPR.htm>

Examples of Enabling Costs

In relation to	Item
Sponsorship related costs	Managerial oversight of study team personnel (such as auditors, clinical monitors, clinical nurses, data managers, pharmacovigilance, bio statisticians)
Sponsorship approval process	Allocation of staff to this for example quality & regulatory manager and pharmacovigilance
	Additional interactions with the finance department for example grant budget development and reviews
	Additional interaction with human resources department such as affiliation review
	Interaction with insurance officer such as confirmation of insurance cover and indemnity
	Interactions with legal/contracts officer for example confidentiality disclosure agreements and clinical trial agreements
	Research support services
	Sponsorship committee
	Sponsor Office(r) – for example risk assessment
Regulatory and ethics submissions	Relevant staff – for example quality and regulatory manager at CRF/C
Facilities	Biobank infrastructure and operation
	Research pharmacy and aseptic compounding units
	IT specific for clinical studies such as software, licences

Survey on Support for Clinicians Across the Academic Sector - Findings and Recommendations

1. Methodology

Three questionnaires were developed for personnel in the research offices/research support services (RO/RSSs), clinical research facilities/centres (CRF/C) and clinicians.

The RO/RSSs questionnaire was sent to the RO/RSS's in the following academic institutions; National University of Ireland Galway (NUIG), Royal College of Surgeons in Ireland (RCSI), University College Cork (UCC), University College Dublin (UCD), Trinity College Dublin (TCD) and (NCRC), Our Lady's Children Hospital Crumlin.

The CRF/Cs questionnaire was sent to the following CRF/Cs; Wellcome - HRB Clinical Research Facility, St. James's Hospital, Dublin, HRB Clinical Research Facility, Galway, HRB Clinical Research Facility, Cork, Royal College of Surgeons Ireland (Beaumont Hospital), UCD Clinical Research Centre (Mater Misericordiae and St. Vincent's University Hospitals), Health Research Institute Clinical Research Support Unit, University of Limerick and Our Lady's Children Hospital Crumlin.

The questionnaires were completed by senior staff in each centre (for example programme/business managers, quality and regulatory affairs manager (QRAM), director/senior research support staff).

Five responses to the RO/RSS questionnaire were received and six responses to the CRF/C questionnaire were received. Two centres (HRI Clinical Research Support Unit UL and NCRC) completed a single questionnaire as those facilities provide both RO/RSS and CRF/C services.

A number of clinicians completed the clinician questionnaire, relating to their current activities in clinical research. Each clinician have joint appointments between the academic institution and the HSE.

In addition to the questionnaires, the feedback and suggestions arising from the clinician panel discussion at the CECR conference (held in May 2018) were incorporated into this report. The panel included a number of clinicians discussing their experience of carrying out clinical research in Ireland, some of the challenges they face and suggestions for possible solutions.

2. Summary of the Results and Outcomes from the Research Offices/ Research Support Services Surveys

Pre-Award Support Services Provided by the RO/ RSS

- Information on funding calls.
- Assistance in the preparation of grant applications.
- Review of proposals / non-scientific aspects of proposals.
- Budgets / costings.
- Training and mentoring of researchers.
- Liaising with / management of engagement with affiliated departments and internal committees.

- Administrative single point of contact for research community; coordination, compliance checks and institutional sign off.

Gaps in Provision of Support for Clinicians Identified by RO/RSS

- More effective communication across clinical research related departments/ functions.
- Better coordinated approach with CRF/Cs.
- Regular interaction/information sessions with clinicians.
- Development of case studies to highlight specific supports.
- Specialised advice such as research design/ methodology, protocol development.
- Advice on requirements for Sponsor related requirements and their costings.

Post Award Supports Provided by the RO/ RSS

- Award management.
- Contract/agreements review.
- Institutional signatory.
- Grant set up.
- Research finance office (supports the financial requirements).
- Research communications.
- Statistics.
- Database management.
- Consultancy management.
- Site visit support and organisation.

Gaps in Provision of Support for Clinicians Identified by RO/ RSS

- More coordination between the RO/RSS and CRF/C.
- Regular meetings.
- Better understanding of the tasks and timelines.
- More defined processes and responsibilities to clarify tasks and timelines.
- More clearly defined roles and responsibilities.
- More effective communication.

Most RO/RSSs reported a low level of coordinated interaction with the CRF/Cs or any interaction was on an informal basis or the interaction was for a specific purpose. For example collaboration to complete the contract review process including patient questionnaires and site agreements and monthly meetings to focus on strategic and policy issues pertaining to clinical research studies.

3. Summary of the Results and Outcomes from the Clinical Research Facility/Centre Surveys

Pre-Award Services Provided by the CRF/C

Advice on specific areas of clinical research:

- Clinical trial design and methodology
- Statistical analysis
- Project management
- Regulatory affairs
- Audit and monitoring
- Pharmacovigilance

- Public patient involvement
- Data management
- Resourcing/clinical research nurse support
- Costings
- Ethics/regulatory aspects
- Protocol requirements
- Insurance
- Governance advice and oversight
- Assess to clinical research infrastructure
- Bio repository
- Quality management
- Sponsorship

While not specifically a support provision, a number of CRF/C representatives mentioned lack of protected time for clinicians as a major impediment to them getting involved in research.

Interaction between the CRF/C and their institutional RO/RSS:

- Varied from none to interaction on specific activities – such as budget, preparation of grant applications, legal/contracts.

Post Award Support Provided by the CRF/C

Support and assistance on:

- Research study initiation, start up, operation and management
- Project management
- Access to resources
- Biostatistical support
- Data management
- Ethics/regulatory submissions and oversight
- Quality management (the QRAM in association with the PI)
- Pharmacovigilance
- Governance oversight
- Pharmacy management
- Monitoring
- Auditing
- Sponsorship activities
- Site file management
- GCP Compliant

Gaps in Provision of Support for Identified by CRF/C

- Some centres identified local gaps in specialised clinical expertise – i.e. Pharmacovigilance, data management, monitoring.
- Gaps in the interaction with the RO/RSS also identified for example in concurrent award management support.
- Interaction with other areas of expertise associated with clinical research – for example health economics.
- Local distribution of overheads income.

- Resources/expertise in study governance structures and management/ availability of a clinical trial manager or support office staff.

Interaction with the RO/RSS in Post Award activities:

- Once a clinical study is confirmed, the CRF/Cs are essentially the main provider of specialist clinical support for post award clinical activities – for example overseeing and operating the study from study start-up and green-lighting and dealing directly with PIs on study-related activities.
- Interaction with RO/RSS is mainly for administrative activities (in conjunction with the chief investigators) primarily related to liaising with the funding agency, award acceptance, grant/award set-up and grant reporting as well as with the contracts/legal (for agreements) and finance (budget review and amendment) and in some cases supporting external reviews.
- The interaction between the RO/RSS and CRF/Cs functions varies across the academic institutions, from none in some cases to cooperation across a range of activities in others.
- In some cases, there is co-operation between a Sponsor Office(r) and CRF/C and the chief investigator in relation to sponsorship and including regulatory requirements and in the “Green Light” process.

Gaps identified in the Interaction between RO/RSS and CRF/Cs in Post Award activities:

- There is a need for a more collaborative approach/better interactions/regular meetings leading to a more clearly defined roles and responsibilities and a framework for oversight and reporting.
- Additional funding to support this interaction and more resources.

4. Outcomes from the Questionnaire to Assess Clinicians Support Needs

A small sample of clinicians were asked to complete a questionnaire relating to their current activities in clinical research and to identify any gaps in the support services provided by their local RO/RSS and CRF/C. The clinicians who responded all had joint appointments between the academic institution and the HSE.

- All of the clinicians used the services of their local CRF/C and also carried out research within the hospital outside their local CRF/C.
- Some responders use the physical infrastructure for some studies and/or some of the services provided by the CRF/C (for example pharmacy).
- As well as leading their own research studies, a number of the clinicians were also engaged in other types of research, including research that is run by Doctor of Medicine Students (Registrars) or other clinical staff.
- They also participated in other studies taking place in the hospital which were coordinated/led by colleagues in other hospitals.
- All of the responders also participated in other research that is not clinical research – (for example audits).

5. Support Services provided by the RO/RSS and CRF/C in your Academic Institution currently using:

At the Study Planning stage:

- Administration support for grant application
- QRAM assisting in the planning stage for a study, including those requiring sponsorship.
- Support/advice relating to sponsorship.
- Advice on resourcing clinical studies
- Supporting activities relating to external sponsorship –facilitating interaction with external sponsor.

At Study Start –Up / during the running/operation of a study

- Legal/ Contracts in relation to agreements.
- RO/RSS post award management and grant/award set-up.
- Using certain facilities of the CRF/C.
- Support during the running of the study.
- Advice/support on sponsorship requirements.
- Regulatory/ethics advice.
- Research nurse support.

Additional supports / support services that would support you in developing / engaging in patient-focused (clinical) research

- Better interaction and more resources to act as an interface between all the departments could make a more cohesive system. (such as interaction between sponsorship hospital legal, RO/RSS legal and contracts, RO/RSS and CRF/C.
- RO/RSS presence in hospitals to provide support and promote face to face interaction with clinicians
- Availability of specialised support services – for example medical advisor, biostatistics, database services
- Access to specialised financial support/advice at the grant preparation stage to ensure projects are adequately costed and budgeted for.
- Dedicated nursing and other resources to be available on an ad hoc basis for short-term studies or specific time basis (for example number of days per week). For example, research nurses who could be paid per project from a central pool of research nurses rather than being employed to work on individual studies
- Supports for studies-related activities after the project end (such as biobanking, transfer of data, publications).
- Administration support for the preparation of grant applications.
- Specific support for sponsor related activities, including requirements for meetings, administrative responsibilities (paperwork).
- Tailored facilities to support meeting the needs of certain patient groups.
- Specialised training/education for staff working with certain patient types.
- Additional funding/redistribution of overhead income to support local activities.
- Standard/suggestive texts for some of the more standard parts of the grant proposal.

- The HRB should consider changing the format of grants they fund to be aligned with European Union funding, where projects are broken down into work packages and a lead PI can delegate tasks for particular work packages. This would take some of the workload away from the lead CI.
- Protected time for clinicians engaged in clinical research. Despite currently having contracts that are 50% service/50% research, in reality the demands for clinical service are such that little time is available for research activities.
- Buyout of PIs time as part of a grant application should be an eligible cost by funders.
- Administration support in the preparation of grant applications.

Clinical Research Support Function

The scoping exercise identified a gap in the provision of research support for clinical research. This section outlines a number of possible roles/activities of a central point of contact for the clinical research community, to coordinate the provision of research support services across the institution and to provide expert specialised knowledge and information pertaining to the planning and conduct of clinical research in the institution and hospital. As the provision of support for clinical research in each institution is different, the delivery of this suggested service could be made by one individual or could be shared across a number of posts/full time equivalents.

Possible Roles/Activities of a Clinical Research Support Function

1. Pre-Award Activities (Liaison / Provision of Professional Advice / Research Support)

Act as the primary point of contact/liaison providing expert specialised knowledge and information on all clinical research related support activities and processes, between the research support services (RSS), the Sponsorship Office (or equivalent) (SO), the clinical research facilities/centres (CRF/C) and the clinical researchers in both the pre-award and initial post award activities.

Liaison

- Co-ordinate the interactions of research support services (provided by RSS (for example RO's and affiliated departments such as finance, human resources, Sponsorship Office (or equivalent) and CRF/Cs) in the provision of support for clinical research.
- Act as the central primary point of contact for clinical researchers (for example be "clinician-facing") in relation to support for their clinical research activities.
- Act as signpost service for clinical researchers to relevant research support services and personnel who provide specialist advice/expertise as applicable.
- Work closely with the respective institutional RO/RSS in the communication of information pertaining to research funding opportunities/activities to the clinical research community (such as clinicians and other healthcare professionals interested in research).
- Act as the liaison/point of contact for clinicians for advice on and guidance through the Sponsorship Approval Process (pre-award). Liaise closely with the RO/SO (as applicable) regarding support and guidance through the sponsorship approval process (pre-award).

Provision of Professional Advice

- Provide guidance to clinical researchers and co-ordinate their interactions with the RSS and CRF/Cs.
- Provide expert advice and support relating specifically to clinical research in the preparation of grant applications. If that advice/support is already provided in an Institution, to coordinate the interaction between clinical researchers and the RSSs available in the academic institution.

- Provide specialist advice on all aspects of clinical research, including identifying funding opportunities, development of grant applications for clinical research (including budgets), grant administration, pre and post-award support, including coordination of ethics and regulatory applications.

Research Support

- Provide hands-on administrative support in the preparation of grant applications, including coordination/management of partners and their submissions to the grant application, completion/compiling support documents for grant applications, compilation of grant applications and uploading to the funder's online systems as required.
- Support and promote institution-wide public patient involvement activities.
- Play a role in training provision/signpost to training provided by CRF/C/institutions human resources/learning and development.

2. Post Award Activities (early / transition stage*)

**Early/ Transition Post Award: This is the period immediately after a research award has been granted, i.e. post award and/or as an initial part of the "Green light" process.*

Coordination of early-stage post award activities on behalf of the PI/CI. This would entail the coordinating of the post award review process by liaising with relevant RSS and institutional departments to ensure activities are completed. Activities could include:

- Award sign-off (in conjunction with RO and/or legal/contracts).
- Negotiation of contracts/agreements (in conjunction with legal/contracts).
- Grant/account set-up (in conjunction with RO/finance).
- Preparation and submission of ethics/regulatory submissions (in conjunction with CRF/C).
- Recruitment of project staff (in conjunction with RO/human resources).
- Study initiation activities (in conjunction with Sponsorship Office), CRF/C).

3. Project Management Activities

- Lead/assist in the setting up, coordination and management of clinical research studies.
- Post study activities for example final reporting requirements, management of on-going activities such as archiving, biobanking.

Proposed Skills and Knowledge required:

- Strong understanding of and experience working in a clinical research environment.
 - Understanding of current Irish medical, academic and health services research environments.
 - Strong knowledge and understanding of the research support environment, including grant writing, pre- and post-award grant activities and management.
 - Understanding of clinical research and clinical trials methodology.
 - Knowledge and understanding of current regulatory requirements governing clinical trials/research, including governance, sponsorship and operational aspects.
 - Knowledge of GCP requirements relating to the conduct of clinical research
 - Excellent leadership, interpersonal and communication skills
 - Strong Project Management skills
 - Excellent planning and organisational skills

Abbreviations

CECR	Corporate Enabling of Clinical Research
CI	Chief Investigator
CIP	Clinical Investigation Plan
CIS	Clinical Indemnity Scheme
CO	Contracts Officer
CRDI	Clinical Research Development Ireland
CRF/C	Clinical Research Facility/Centre
CRF	Case Report Forms
CRN	Clinical Research Nurses
CRSU UL	Clinical Research Support Unit University of Limerick
CSRF	Clinical Study Registration Form
CTA	Clinical Trial Agreement
CTN	Clinical Trial Network
DESCA	Development of a Simplified Consortium Agreement
DoH	Department of Health
DORT MD	Division of Responsibilities Table Medical Devices
DORT MP	Division of Responsibilities Table Medicinal Products
DSA	Delegated State Authorities
DSMC	Data Safety and Monitoring Committee
ECRIN	European Clinical Research Infrastructure Network
EI	Enterprise Ireland
FEC	Full Economic Costing
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
HEIs	Higher Education Institutions
HPRA	Health Products Regulatory Authority
HRB	Health Research Board
HRB CRCI	Health Research Board Clinical Research Coordination Ireland
HSE	Health Service Executive
IDMC	Independent Data Monitoring Committee
IMD	Investigational Medical Device
IMP	Investigational Medicinal Product
IP	Intellectual Property
IPoC	Insurance Point of Contact
ISFs	Investigator Site File(s)
KTI	Knowledge Transfer Ireland
MD	Medical Devices
MP	Medicinal Products
NCRC	National Children's Research Centre
NHS	National Health Service

NUIG	National University of Ireland Galway
PI	Principal Investigator
QRAM	Quality and Regulatory Affairs Manager
RCPI	Royal College of Physicians Ireland
RCSI	Royal College of Surgeons Ireland
RO/RSS	Research Office/Research Support Service
SAE	Serious Adverse Events
SAP	Statistical Analysis Plan
SCA	State Claims Agency
SFI	Science Foundation Ireland
SIG	State Indemnity Guideline
SmPc	Summary of Product Characteristics
SO	Sponsor Office(r)
SOC	Sponsorship Oversight Committee
SOCR	Sponsorship Oversight Committee Report
SOP	Standard Operating Procedures
SOT	Study Operational Team
SPG	Study Planning Group
SRA	Sponsorship Risk Assessment
SRAF	Sponsorship Risk Assessment Form
SSO	Sponsor Signatory Official
SUSAR	Suspected, Unexpected Serious Adverse Events
TCD	Trinity College Dublin
TMF	Trial Master File
UCC	University College Cork
UCD	University College Dublin
UL	University of Limerick
WG	Working Group
WGs	Working Groups

For more information contact
info@crdi.ie
www.crdi.ie/corporate-enabling-of-clinical-research