Research & Development
Taighde & Forbairt

HSE National Framework for Governance, Management and Support of Health Research

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Seirbhís Sláinte Níos Fearr á Forbairt | Building a Better Health Service

Contents

Glossary of key terms

The following terms have the meaning indicated below for the purpose of this document:

Clinical trial: A clinical trial is a type of health research. These types of studies prospectively assign human participants or groups of humans to one or more health-related intervention in order to evaluate the effects on health outcomes. Interventions include, but are not restricted to, drugs, cells and other biological products, surgical procedures, radiological procedures, devices, behavioural treatments, process-of-care changes, or preventive care. The term 'clinical trial' in this Framework includes regulated and non-regulated trials as well as clinical investigations of medical devices.

Regulated clinical trials or medical device investigations are those that fall under the remit of the competent authority, which in Ireland is the Health Products Regulatory Authority (HPRA), in other words, such trials require HPRA approval.

Clinical trials of investigational medicinal products (CTIMPs) are governed by The European Clinical Trials Directive 2001/20/EC,[1] which was transposed into domestic Irish law by The European Communities (CTMP) 2004 Regulations.[2] The European Clinical Trials Directive 2001/20/EC and the European Communities (CTMP) 2004 Regulations[3] are soon to be replaced by the European Clinical Trials Regulations No536/2014[4] (and accompanying domestic secondary legislation), which is expected to come into effect in 2021.

Clinical investigations of medical devices are governed by the European Medical Devices - Regulation 2017/745/EC[5] on medical devices, amending the European MP- Directive 2001/83/EC,[6] the European EFSA - Regulation 178/2002/EC[7] and the European CP-Regulation1223/2009,[8] and repealing the Council AIMD Directives 90/385/EEC[9] and the Council MD- Directive 93/42/EEC[10] (and accompanying domestic

1 DIRECTIVE 2001/20/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (OJ L 121, 1.5.2001, p. 34); https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:121:0034:0044:en:PDF

2 S.I. No. 190/2004 - European Communities (Clinical Trials on Medicinal Products For Human Use) Regulations, 2004;

3 S.I. No. 190/2004 - European Communities (Clinical Trials on Medicinal Products For Human Use) Regulations, 2004;

4 REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC ((OJ L 158/1, 27.5.2014, p. 34); https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

5 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (OJL 117, 5.5.2017, p1-175).

6 Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. *OJ L 311, 28.11.2001, p. 67–128. https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32001L0083*

7 Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety *OJ L 31, 1.2.2002, p. 1–24 https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32002R0178*

8 Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products (Text with EEA relevance)OJ L 342, 22.12.2009, p. 59–209. *https://eur-lex.europa.eu/legal-content/en/ALL/?uri=CELEX%3A32009R1223*

9 Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devicesOJ L 189, 20.7.1990, p. 17–36. *https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A31990L038*

10 Council Directive 93/42/EEC of 14 June 1993 concerning medical devices *OJ L 169, 12.7.1993. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31993L0042*

secondary legislation). In both cases, the legislation makes compliance with good clinical practice guidelines a legal requirement for study conduct.

By contrast, non-regulated trials could be interventions such as exercise programmes, physiotherapy, surgical procedures, complementary medicine, or behavioural interventions. Advice should be sought from the HPRA if in doubt about whether a clinical trial is regulated or non-regulated.

Good Clinical Practice (GCP) and Good Manufacturing Practice (GMP): Good Clinical Practice (GCP) is a set of internationally recognised ethical and scientific quality standards for the design, conduct, recording and reporting of clinical trials that involve humans. Good Manufacturing Practice (GMP) describes the minimum standard that a medicines manufacturer must meet in their production processes. Compliance with GCP and GMP standards[11] provides public assurance that the rights, safety and well-being of trial participants are protected, and that the results of the clinical trials are credible and accurate.

Health research: Health research is defined in alignment with Regulation 3.(2) of S. 36(2)(Health Research) of the Data Protection Act 2018[12] as:

(i) "research with the goal of understanding normal and abnormal functioning, at the molecular, cellular, organ system and whole body levels;

(ii) research that is specifically concerned with innovative strategies, devices, products or services for the diagnosis, treatment or prevention of human disease or injury;

(iii) research with the goal of improving the diagnosis and treatment (including the rehabilitation and palliation) of human disease and injury, and of improving the health and quality of life of individuals;

(iv) research with the goal of improving the efficiency and effectiveness of health professionals and the health care system;

(v) research with the goal of improving the health of the population as a whole or any part of the population through a better understanding of the ways in which social, cultural, environmental, occupational and economic factors determine health status".

11 European Clinical Trials Directive 2001/20/EC and European GCP (Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products (Text with EEA relevance, *OJ L 91, 9.4.2005, p. 13–19. https://eur-lex.europa.eu/eli/dir/2005/28/oj*

12 S.I. No. 314/2018 - Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018; http://www.irishstatutebook.ie/eli/2018/si/314/made/en/print

It is a broad definition, which includes experimental, health and health services, translational and clinical research (including clinical trials, observational studies, behavioural, public health and social care research, population health research, basic and translational health research, research into treatment strategies, and medical device or product development). It also includes any actions taken to establish whether an individual may be suitable for inclusion in the research.

Public and Patient Involvement in Research: Public involvement in research is research carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them. It may range from informing, to co-development and empowerment, and it means working in collaboration or partnership with patients, families, carers, service users or the public in planning, designing, managing, conducting, dissemination and/or translation of research. PPI is a requirement for some health research funding bodies.

Research participant: Any individual who consents to take part in a research study (in law, participants in clinical trials involving medicines are known as subjects).

Abbreviations

CECR	Corporate Enabling of Clinical Research
CIS	Clinical Indemnity Scheme
CRF/C	Clinical Research Facility/Centre
CRO	contract research organisation
CTIMPs	clinical trials of investigational medicinal products
DPIA	data protection impact assessment
DSA	delegated State authority
DPO	Data Protection Officer
GCP	good clinical practice
GDPR	General Data Protection Regulation (EU) 2016/679
GIS	General Indemnity Scheme
GMP	Good Manufacturing Practice
HG	Hospital Group
HPRA	Health Products Regulatory Authority
HRB	Health Research Board
HRCI	Health Research Charities Ireland
HSE	Health Service Executive
NIMS	National Incident Management System
NREC	National Research Ethics Committee
PI	principal investigator
PPI	Public and Patient Involvement
R&D	Research and Development
REC	Research Ethics Committee
RGMS	research governance, management and support
SCA	State Claims Agency
SUSARS	Suspected Unexpected Serious Adverse Reactions

Executive Summary

The HSE framework for the Governance, Management and Support of Research (RGMS framework) seeks to protect research participants by ensuring that the research activity we host is ethically sound, and that the participants' data will be protected and safe. It also aims to facilitate research for staff and collaboration with academic institutions while allowing the HSE to comply with its legal and regulatory obligations, which is, in turn, essential to guarantee public trust.

The framework highlights the importance of patients as equal partners in the research process and the value of Patient and Public Involvement (PPI) in research. PPI can increase the value and relevance of research by focusing on questions and priorities of importance to patients and their families, increasing recruitment into studies, shaping study design, and assisting with analysis by providing insight and the patient perspective. PPI involvement can also inform the dissemination process by connecting with patient organisations, and can help to avoid wasteful practice.

The RGMS framework is built around the following key principles:

- Research activity needs to be registered and risk assessed before it commences.
- Research ethical opinion should be independent and separate from institutional governance.
- Institutional governance for individual research studies should be proportionate to the level of risk.
- Both ethical and governance approval is required before proceeding.
- The roles and responsibilities of the various parties involved in research studies need to be articulated and agreed before the research commences.
- Research studies need to comply with relevant legislation and regulatory requirements.
- Oversight is required through the lifetime of the research study.
- Research participants and patients are key partners in the research process and their opinions and needs should be considered throughout the life cycle of the research.

The implementation of the RGMS framework represents a stepping-stone towards nurturing a research culture in the HSE and recognising that research is a crucial activity, which contributes to the improvement of services and benefits patients, their families and the public.

Its full implementation will require both reform of the HSE Research Ethics Committee system as well as the development of capability for research management and support within the service. This will include the establishment of Research and Development offices through our organisation that will facilitate collaboration between different legal entities (i.e. HSE services, Section 38 and 39 organisations, academic institutions, health charities) and will help staff to navigate the complex regulatory environment of health research. Implementation will also require the development of additional HSE national research related policies, protocols and the establishment of formal agreements with academic institutions to streamline processes and clarify roles and responsibilities.

This framework is a key output of the *HSE Action Plan for Health Research 2019–2029*[13] and it has received the support of a large range of stakeholders. While consultation on the development of the framework has been significant, it is acknowledged that it represents a significant programme of change and that challenges will be identified. Hence, this will be a "living framework" over the next five years, so that lessons learned by implementation can be formally incorporated on an annual basis while collaborating with patient representatives in the review and amendment process.

13 Terrés AM. HSE Action Plan for Health Research 2019–2029. Dublin: Health Service Executive; 2019. Available from: http://hdl.handle.net/10147/626952

1 Introduction and context

1.1 Introduction

International evidence indicates that health services where research is formally integrated as part of the organisational structure, delivers better care.[14] Research enables evidence-based practice, and together with innovation, teaching and training, is essential in order to deliver the best patient outcomes. These elements need to be considered in the development of health policies, and in this context, the *HSE Action Plan for Health Research 2019–2029* outlines the roadmap to follow in order to embed research and innovation into the culture of the public health service.

This *HSE Framework for the Governance, Management and Support of Researc*h is the first output of the *HSE Action Plan for Health Research 2019–2029*. **It aims to create clarity and establish a cohesive national approach for effective and efficient processes in the management, governance and support of research in the Health Service Executive (HSE) and its funded organisations.** A wide range of clinical and non-clinical staff members are engaged in research and much is enabled through engagement with third-level institutions.[15] Health service delivery organisations have a responsibility to manage risks and ensure that research involving service users, their samples or their data is safe and conducted to best practice standards and in compliance with legislation. It is also good practice that procedures exist for partnership with patients, their families and carers, service users and the public in the design, management, conduct and dissemination of research.

The principles in this Framework are intended to deliver a step change that will contribute to establishing a culture of research and innovation in the Irish health service for the good of patients, their families and carers, staff, the public and the economy. Researchers strive to develop new and better treatments, to improve health and health services, and to tackle the challenges of an ageing population. Changes in healthcare are inevitable, following the development of new technologies ranging from the Internet, social media and rapid access to information, to artificial intelligence, genomics, immunology, imaging, and many other scientific advances. As new technologies develop, this will drive important changes in society. Therefore, we need to address these key drivers in the service that we deliver.

As new legislation is introduced, there is now more than ever, a need for a clear research governance pathway that enables research and protects the safety and interests

14 Boaz A, Hanney S, Jones T, Soper B. Does the engagement of clinicians and organisations in research improve healthcare performance: a three-stage review. BMJ Open. 2015;5:(12):e009415. Available from: https://doi.org/10.1136/bmjopen-2015-009415

15 Terrés AM, O'Hara MC, Fleming P, Cole N, O'Hanlon D, Manning P. Research Activity in the HSE and its Funded Organisations: a report of staff engaged in research, research studies undertaken, publication output and research networks. Dublin: Health Service Executive; 2019). Available from: http://hdl.handle.net/10147/626953

of research participants and staff, without introducing unnecessary confusion or complexity. Furthermore, patients, carers, families, service users and the public should be given the opportunity to be involved in the planning, design, conduct, management, dissemination and translation of research. PPI can increase the value and relevance of the research by focusing on questions and priorities that are of importance to patients and their families, which can help to avoid wasteful practice.

It is recognised that organisational capability needs to be built within the HSE and its funded organisations in order to implement the requirements of this Framework, and that a phased implementation approach will be required. **Hence, it is important that organisations make interim arrangements to support, rather than hinder, research while the full implementation of the Framework is taking place.** This is also an opportunity to build on and further develop robust collaborative links with third-level institutions and industry sectors, patients, research charities and other key stakeholders within the national health research system.

The implementation of this Framework will provide the opportunity to streamline, standardise, simplify and harmonise procedures for approval of research studies, and to showcase research activity while providing the context for the encouragement of creative and innovative research and for the effective transfer of learning, technology and best practice to improve care.

1.2 Context

This Framework addresses the recommendations of *Governance of Research in the HSE and HSE Funded Healthcare Services: A Scoping Report* (January 2019),[16] which identified the lack of a HSE health research governance framework as one of the biggest gaps in the sustainability and development of research activity in the HSE.

In early 2017, Irish third-level institutions and research funders came together under the Corporate Enabling of Clinical Research (CECR) initiative to identify and address the challenges of sponsoring and supporting clinical research studies in Ireland. The CECR report[17] summarises the outputs and recommendations delivered by six working groups. The implementation of this Framework provides the opportunity to build a tailored system, which incorporates the lessons learned from the outputs and CECR working groups' recommendations.

This Framework for governance, management and support for research in the HSE sets out, for the first time, tailored principles of good practice in the management and conduct of health research for the HSE. It is aligned with international practice and its

16 Terrés AM, Cole N, O'Hanlon D, O'Hara MC, Dever S. Governance of Research in the HSE and HSE Funded Healthcare Services: A Scoping Report. Dublin: Health Service Executive; 2019). Available from: http://hseresearch.ie/wp-content/uploads/2020/05/Governance-of-Research-in-the-HSE-and-HSE-Funded-Healthcare-Services.-A-Scoping-Report-compressed.pdf

17 Corporate Enabling of Clinical Research Report. 2019) https://crdi.ie/wp-content/uploads/2019/10/CECR-WEB.pdf. Available from: https://crdi.ie/wp-content/uploads/2019/10/CECR-WEB.pdf

implementation will address the critical issues that have been identified.

The implementation of this Framework will be supported by further outputs from the HSE Research Governance, Management and Support Framework Implementation Working Group[18] and will take place in tandem with the **reform of the HSE Research Ethics Committee (REC) system**.[19] The successful implementation of both this Framework and REC reform will pivot around the implementation of a **national research information management system** to enable an efficient and effective process for both ethical and governance review and approval.

1.3 Overall purpose

The overall purpose of this Framework is to set out clear principles for the implementation of best practice for the governance, management and support of research in the HSE and in HSE-funded organisations providing public health and social care services in Ireland. This Framework also clarifies the roles and responsibilities of the different parties involved in research, articulates the review and authorisation processes required before and after the research commences, and outlines the organisational structures required to put it into practice.

The implementation of this Framework will ensure that research is underpinned by a commitment to best practice, ethical values, regulatory and legal requirements, patient and public involvement and will contribute to embedding research activity within health service delivery for the benefit of service users and staff.

1.4 Scope

This Framework applies to all health research[20] activities taking place in the HSE and its funded organisations involved in the provision of health and social care services, when the research activities involve any of the following factors: health service users, their personal data and/or their biological samples, health and social care staff, or the use of healthcare services, premises or infrastructure. It also applies to health research taking place in third-level collaborative institutions and/or clinical research facilities (CRFs) when the research activities involve any of the aforementioned factors.

18 The HSE Research Governance, Management and Support Framework Implementation Working Group was established in 2020 to fine-tune the first draft of the Framework by taking into account the constraints and realities of implementation, and to develop the roadmap and practical detailed guide for implementation. Membership includes directors of research from Hospital Groups and other key representatives from hospitals, universities and national services.

19 A summary roadmap for the reform of the HSE Research Ethics Committee system is included in Appendix 3.

20 See definition of 'health research' in the Glossary of key terms.

This Framework is relevant to:

- the HSE and its funded healthcare provider organisations that are involved in leading, hosting, sponsoring and/or approving research activity,
- collaborative third-level institutions, industry, and other research partners and stakeholders involved in collaborative activities with the HSE and/or its funded organisations,
- RECs providing ethical review services to research taking place in the HSE,
- linked health and social care delivery organisations, or any third-party involving any of the factors mentioned above,
- all third-party researchers performing research activities involving the factors mentioned above,
- patients, advocate groups and health service users who may participate in research studies or be patient partners in the design, planning, conduct, management, dissemination and translation of research,
- health research funders and health research charities that fund, manage or direct research.

For the avoidance of doubt, the scope of this Framework does not extend to clinical audits, standard service evaluations, public health work, or advanced health analytics carried out by the HSE and its funded organisations for the purpose of discharging their legal obligations for the planning and delivery of health and social care services.

1.5 Responsibilities of staff and organisations

Hospitals, community services and national services are responsible for the research studies that they host, and are therefore responsible for the implementation of this Framework and for ensuring that staff members are appropriately informed of the local requirements. Services that have strong collaborative links with third-level institutions are responsible for implementing collaborative and coordinated approaches, which promote consensus and avoid duplication of effort.

Services are also responsible for bringing awareness of this Framework to the attention of any external stakeholders (e.g. third-level institution collaborators, contract research organisations, industry partners, health research charities) who engage with the HSE or any of its funded health and social care service providers for the purpose of health research. Staff need to familiarise themselves with the local requirements for research approval and oversight, and comply with relevant standardised protocols.

1.6 Framework development process

The development of this Framework has been led by the HSE National Office for Research and Development (R&D), with the support of a **working group of key stakeholders** (Appendix 1). The Framework incorporates best international practice and lessons learned in other jurisdictions, and it has undergone **extensive internal and external consultation** with, inter alia, the Department of Health, the HSE Data Protection Office [including the Data Protection Officer (DPO) and the Deputy DPOs], the State Claims Agency (SCA), the Health Products Regulatory Authority (HPRA), university vice-presidents for research, the Health Research Board (HRB), Enterprise Ireland, industry representatives, the chief executive officers of the Hospital Groups (HGs) and the Board of Clinical Research Development Ireland (inclusive of directors of academic CRFs).

Patient perspectives were provided by, Health Research Charities Ireland (HRCI), the HSE National Office for R&D PPI Advisory Group and the HSE Quality and Patient Safety Committee.

2 Organisational structures required for supporting, approving and overseeing research in the HSE

The implementation of governance and provision of management and support services for research in the health and social care services requires specialised organisational structures, which include the RECs and the Research Governance, Management and Support (RGMS) functions.

2.1 Research ethics committees

Research Ethics Committees (RECs) are a fundamental cornerstone in the overall process of governance of health research. The role of the REC is to provide an independent opinion in relation to the ethical aspects of research proposals. As of January 2021, the RECs in the health service operate individually, and are part of a fragmented system with multiple approaches to the process of research ethics committee approval. This is problematic, as it creates RECs of varying expertise and resourcing, and it contributes to significant unpredictability and inconsistency in terms of REC decision-making.

The establishment of National Research Ethics Committees (NRECs),[21] as well as the requirements articulated in the Data Protection Act 2018, represent an opportunity to bring about the urgently needed reform of the REC system servicing the health service.

The HSE National Office for Research and Development in collaboration with the HSE REC Reform Working Group[22] are currently developing a high-level roadmap (Appendix 3) for such reform. This roadmap aims to establish a PPI informed, effective, efficient and transparent REC system in the HSE and associated organisations, so that it is in line with the NRECs and newly developed RGMS functions for health research in the HSE.

21 The National Office for Research Ethics Committees was established in 2020, and its primary function is to deliver a robust and transparent system for NRECs. The first NRECs to be established will deal with clinical trials for investigational medicinal products, clinical investigations of medical devices, and studies involving ionising radiation, and will enable Ireland to comply with the EU regulations in these areas.

22 The HSE Reform working group was established in 2020 with the objective of developing a standard Code of Practice for HSE RECs and a roadmap for the reform of the HSE REC system. The group include representatives from HSE and S38 RECs as well as patient representatives.

2.2 Research governance, management and support function

Governance, management and support of research in the HSE and its funded organisations requires the development of resources and functions with such responsibilities. While some capacity already exists in some hospitals and HGs, in addition to strong collaborative links with third-level partner institutions in certain cases, further capacity needs to be developed internally within the health service to ensure that healthcare providers have appropriate oversight of the research that they host and for which they are responsible.

The responsibility of the RGMS function is very different to the responsibility of the REC. While the REC is concerned with ethical considerations and the rights of the participants in each research study submitted for evaluation, the RGMS function provides organisational oversight to ensure that healthcare services manage the relevant organisational risks as appropriate and comply with their research, legal and financial obligations. The role of this function can be summarised as follows:

Research governance: provides organisational oversight for research that takes place in collaboration with, or independently of, third-level institutions. The function deals with issues related to research misconduct, and provides a reporting line for research activities that take place within the organisation.

Research management: provides the necessary approval and authorisation for research that takes place in collaboration with, or independently of, third-level institutions and provides ongoing oversight for research activities up to when the research study can be deemed closed (which may be past the study end date due to research and other audit requirements). It includes the assessment and management of the many aspects of any research study, including but not limited to legal, financial, staffing, data protection, intellectual property, sponsorship, liability and indemnity, risk management, both before and during the research study life cycle.

Research support: (a) provides HSE researchers with assistance and training to navigate the complex regulatory frameworks and landscape that relate to the conduct of health research, and (b) provides support and training to HSE and non-HSE researchers on compliance with HSE policies and local standard operating procedures. It also creates the organisational infrastructure to support research collaboration internally and externally with third-level institutions and the private sector. It supports, trains and guides researchers in their partnerships with patients and patient organisations throughout the research cycle.

A proposed approach for the design of the RGMS function in various settings is included in Appendix 4. This model was developed in collaboration with the HSE Research Governance Framework Implementation Working Group, which includes representation from all HSE Hospital Groups and other key stakeholders.

3 Key roles and responsibilities in relation to governance, management and support of research

A number of key roles are essential for the responsible conduct of research within an appropriate governance, management and support framework during the research life-cycle. These roles are outlined below and further detailed in Appendix 2.

The responsibilities of each of these parties should be articulated and agreed for each study before the research commences.

3.1 Responsible legal entity

A responsible legal entity is the body that, either alone or with another entity, has ultimate responsibility for the study. The term 'sponsor' is used for the responsible legal entity for clinical trials. For other types of studies, the legal responsibility for the various aspects of the study (e.g. contractual, financial, data protection), may reside with one or several parties [i.e. the organisation responsible for accepting and managing the research funding, the clinical investigators and their employers, and the data controller(s) may be any one or all of the participating organisations]. Data Protection Law requires clear, factual and formal identification of controllership (e.g. sole / separate / joint controllers, data processors).

3.1.1 Sponsor

In alignment with the HRB's *Clinical Trials and Interventions Research Governance Policy*, the term 'sponsor' in this Framework **is defined as "the legal entity which has ultimate responsibility for the study and compliance with the regulations, principles and standards of good practice that governs clinical research"**.[23] It applies to clinical trials and interventions, as defined in the glossary of key terms and includes regulated and non-regulated trials. The sponsorship responsibilities for CTIMPs and clinical investigations of medical devices are governed by legislation.[24]

23 Health Research Board. Clinical Trials and Interventions Research Governance Policy. Available from: https://www.hrb.ie/funding/funding-schemes/before-you-apply/all-grant-policies/clinical-trials-and-interventions-governance/

24 See footnotes 1-19. For information please visit the HPRA website.

The sponsor (as the legal entity) takes responsibility for the initiation, management, financing (or arranging the financing) and reporting of the clinical trial and interventions, but the principal investigator conducts the investigation. The sponsor is responsible for ensuring appropriate inclusion of patient, service user and public involvement in a study, and for providing access to the relevant training and support. The sponsor also accepts responsibility as data controller for the clinical trial, and **for ensuring that appropriate insurance or indemnity is in place to cover liabilities, which may arise in relation to the design, management and conduct of the clinical trial or intervention.**

The sponsor may delegate some responsibilities to qualified third-parties, and this must be appropriately documented. The sponsor retains ultimate responsibility for the quality and integrity of the study data and must ensure oversight of all delegated activities.

All clinical trials must have a sponsor regardless of the level of risk. A sponsor can be a third-level institution, a hospital, a pharmaceutical company or another legal entity.

The level of oversight required during the implementation of the clinical trial should be assessed carefully and be commensurate with the clinical trial's risk level. All oversight arrangements must be disclosed at the time of proposal registration with the RGMS function. All parties collaborating on the research study must, prior to starting the study, enter into an agreement that defines the roles and responsibilities of each of the collaborating organisations in the research study based on a factual analysis of their participation and the participation of their employees. Any subsequent changes made to the sponsorship arrangements during the lifetime of the research study must be notified to the relevant RGMS function and captured in an amendment to the above mentioned agreement.

The responsibilities of sponsors are very significant. Therefore, public hospitals and other health and social care providers, should only take on the role of sponsor of clinical trials and interventions **if they have developed appropriate RGMS functions to a maturity level that allows the organisation to provide appropriate sponsorship oversight commensurate with the level of risk and complexities of the research study, or when they are in the position to delegate these responsibilities appropriately with the agreement of the delegated entity or organisation.** The role of sponsor cannot be assumed by default (e.g. a clinical trial cannot commence without approval on the assumption that the principal investigator's employer is the default sponsor), and the RGMS function should carefully assess the organisation's ability to deliver on the sponsor role.

3.1.2 Responsible legal entity/entities for research other than clinical trials

For research other than clinical trials, one or more legal entity may be responsible for the various aspects of the research study. They may include the following:

- the employer or employers of the researchers,
- the organisation that accepts the research funds and establishes a contractual relationship with the funder,
- the data controller and processor,
- the researchers themselves in certain circumstances.[25]

As there may be one or more legal entities, it is therefore essential that the responsibilities of each entity with regard to the different aspects of the research study are articulated and agreed in advance. These aspects include:

- financial responsibility,
- responsibility for the indemnity and insurance for the research,
- responsibility for compliance with data protection legislation,
- responsibility for research misconduct,
- responsibility for rights related to intellectual property generated from the research,
- responsibility for compliance with HSE policies and procedures and other standards of good practice.

3.2 Principal investigator, co-principal investigator, chief investigator and collaborator

The principal investigator (PI) is responsible for the day-to-day management of the research study at the research site. The PI retains ultimate responsibility for the management of the research study, even if tasks are delegated to other research staff.

The PI is responsible for all research activities at the site. These responsibilities include ensuring that the study is conducted in accordance with all regulatory requirements including compliance with GCP (for clinical trials) and GMP, data protection legislation, and with all the relevant HSE national and local policies and governance protocols as they apply to the research activity. It has to be pointed out that a data controller is determined as a matter of fact on the basis of the particular circumstances that apply. If, as is usually the case, the data controller is not the PI, the actual controller cannot escape its responsibilities by assigning them all to the PI.

Where HSE staff hold a dual affiliation, they must decide which organisation (i.e. the HSE or the academic/other organisation) they will represent for the entire duration

25 For example, when the researcher acts in a private contractor capacity, such as a general practitioner (GP).

of the research study, and this determination must be done and confirmed in writing with the RGMS before the start of the research study. This is a vital requirement for the correct determination of controllership between the collaborative organisations.

In the case of multisite studies, the lead researcher who takes overall responsibility for the research study is referred to as the **chief investigator**, and the lead researcher within each site is referred to as the PI. If there is more than one PI at one site, they are referred to as co-PIs. All **co-PIs** have the same PI responsibilities, as described above. Other investigators involved in the research study, but who do not share the PI responsibilities, may be referred to as **collaborators**.

3.3 Research site (host site)

A research site is a facility, location or service (e.g. hospital) where the research is being conducted. This includes:

a) the organisation or organisations where the research is taking place, and/or,
b) the organisation who's service users, patients or staff are involved in the research and/or,
c) the organisation that provides research staff, primary data, infrastructure or premises to facilitate the research.

When research is taking place across academic Clinical Research Facilities/Centres (CRFs/Cs) and hospitals, the associated hospital would generally be considered to be the research site.

3.4 Research site responsible officer

External research studies (i.e. third-level institution projects led by a PI who is not a member of staff) taking place within a research site should involve an employee of such a site (i.e. research site responsible officer). The level of involvement will depend on the nature of the research study and the responsibilities and requirements placed on such an employee of the site.

The research site responsible officer could be a co-PI, a collaborator, a site access supervisor, or a provider of access to data. Regardless of the level of involvement, this person will ensure that, at a minimum, the research taking place at the site is conducted in a manner that complies with the requirements of this Framework and with any relevant local protocols, and HSE policies. The PI must be an employee of the HSE or funded organisations if insurance is to be provided by the SCA scheme (see Section 3.9). For all other scenarios, additional insurance and indemnity cover certificates will have to be provided.

The specific roles and responsibilities of the research site responsible officer for each study should be articulated at the time of study registration with the RGMS function.

3.5 Research Ethics Committees

RECs are responsible for the independent assessment of all ethical considerations of a study before the study can commence. They are also responsible for ongoing oversight of research studies when amendments or changes to the original protocol or other relevant study documentation are required, or when safety issues arise. RECs are normally established by the HSE, hospitals, or third-level institutions, and there should be formal legal documentation underpinning the establishment and operation of a REC, in particular addressing composition, governance, indemnity and independence matters. A further description of RECs' role is included in Section 4.1.

3.6 Health Products Regulatory Authority

The HPRA is the agency in Ireland responsible for the regulation of CTIMPs and regulated clinical investigations of medical devices. The HPRA requires that all regulated clinical trials and investigations are designed, conducted and reported in accordance with the principles of GCP and in compliance with all relevant legislation (e.g. clinical trials of medicinal products and clinical investigations of medical devices legislation, or GMP).

3.7 Research funders

The funder is the organisation or group of organisations providing funding for the research study. They can be commercial or non-commercial (i.e. national, international or EU funding agencies, philanthropy sources and research charities).

3.7.1 Commercial funders

Commercial funders generally take on the sponsor role and they dictate the purpose of the study and the terms and conditions of participation. Commercial funders/ sponsors are expected to provide assistance with any enquiry, audit or investigation related to the funded work.

3.7.2 Non-commercial funders

Non-commercial funders generally fund investigator-led studies. Through their competitive peer-reviewed awarding processes, they establish whether the research proposal can be funded based on pre-determined criteria (e.g. high scientific quality, management, socio-economic impact, scientific and translational impact, value for money). They should do this via an independent expert review that assesses:

- the quality of the research as proposed,
- the experience and expertise of the PI and other key researchers,
- whether there is appropriate research infrastructure for the study: for example, management and governance arrangements; access to potential participants (or their organs, tissue or data); specialised facilities, such as equipment, materials or support staff; and, for clinical trials on medicines, expert clinical trial management and the capacity to comply with the principles of GCP,
- the societal and economic impact of the study,
- the quality of PPI approach for the research,
- other criteria that may be specific to the call for proposals.

3.8 Employers

Employers are defined as the organisations employing the PI and members of the research team. Employers are responsible for the actions of their employees, and they should have governance arrangements in place that ensure that they are always aware of what activities their employees are engaged in, especially employee activities that involve working with third-parties. Many different arrangements may impact on the role of an employer in relation to a specific research activity, and it is therefore essential that the employer's responsibilities are articulated clearly at the time of research study registration.

Employers are expected to:

a) encourage a high-quality research culture,
b) provide appropriate governance of the research for which they are responsible,
c) ensure that researchers understand and fulfil their responsibilities,
d) take proportionate, effective action in the event of errors and breaches, or if misconduct or fraud are suspected,
e) ensure that research activity does not interfere with the delivery of health and social care services in the relevant site,
f) provide adequate training to their employees and registered students on good research practice, research integrity, and data protection,
g) ensure employees and students conducting research have been Garda vetted prior to conducting health research.

3.9 State Claims Agency

Under the National Treasury Management Agency (Amendment) Act 2000,[26] the National Treasury Management Agency (Amendment) Act 2014 and various Delegation Orders, the management of claims for personal injury, property damage and legal costs against delegated State authorities[27] (DSAs), and of the underlying risks, was delegated to the National Treasury Management Agency. When performing these functions, the National Treasury Management Agency is known as the State Claims Agency (SCA).

The SCA operates two schemes:

- Clinical Indemnity Scheme: this refers to the scheme under which the SCA manages personal injury claims arising from the provision of, or the failure to provide, professional medical services by those State authorities and persons covered by the scheme.
- General Indemnity Scheme: this refers to the scheme under which the SCA manages personal injury and property damage claims against certain State authorities covered by the scheme.

The definition of professional medical services includes the conduct of research – S.I. No. 628/2007 – National Treasury Management Agency (Delegation of Functions) (Amendment) Order, 2007.[28] The SCA provides indemnity cover to the HSE and delegated State Authorities (DSAs) for health research as follows:

Clinical Indemnity Scheme (CIS):

- CIS cover automatically applies to DSA-approved non-interventional health research that is conducted by DSA staff in a DSA premises where the trial/research subjects are HSE patients.
- Health research undertaken as part of third-level institution research studies, i.e. PhD/MSc studies, is subject to the requirements of the HSE Framework for the Governance, Management and Support of Research. Patient interventions must be supervised by a DSA clinician in order for the CIS to apply. Other appropriate insurance may be required and must be provided by the third-level institution.
- A number of conditions must be met in order for the CIS to apply to clinical trials, interventional trials, or studies and regulated research where there is a third-party sponsor, e.g. a third-level institution, pharmaceutical company or other commercial company. This includes research ethics approval, a DSA clinician acting as the PI, a signed clinical trial indemnity form, and clinical trial insurance

26 National Treasury Management Agency (Amendment) Act, 2000; http://www.irishstatutebook.ie/eli/2000/act/39/enacted/en/html
27 For a list of delegated State authorities, visit the SCA website at https://stateclaims.ie/about-our-work/state-indemnity/sca-delegated-authorities.
28 S.I. No. 628/2007 – National Treasury Management Agency (Delegation of Functions) (Amendment) Order, 2007; http://www.irishstatutebook.ie/eli/2007/si/628/made/en/print

and product liability cover with adequate limits of indemnity. These conditions must be verified by the SCA or a designated representative of the SCA.

- In situations where a DSA acts as the sponsor of clinical trials, interventional trials or studies, or regulated research, there may be added insurance requirements independent of the General Indemnity Scheme/CIS cover, e.g. product liability insurance, or no fault compensation. Please contact the SCA for further guidance.

General Indemnity Scheme (GIS):

- GIS cover applies to the health research activities of a DSA and its staff. External parties must have their own insurance in place to cover the activities of their organisation/staff, i.e. employers' insurance and public liability insurance policies with adequate limits of indemnity.

Further details and guidance can be found at www.stateclaims.ie, or by emailing the SCA: stateclaims@ntma.ie

3.10 Data controller

The role of data controller is outlined in the General Data Protection Regulation (GDPR),[29] and additional obligations on data controllers apply in the context of health research. These additional obligations are outlined in S. 36(2)(Health Research) of the **Data Protection Act 2018**[12] and subsequent amendments. Legal responsibility for complying with the Data Protection Law is the responsibility of the Controller.

- **The HSE is always the data controller of the personal data it holds for the** performance of its statutory functions, including the **provision of healthcare**. An employee of the HSE will act as an employee of the data controller in the normal course of their duties (i.e. healthcare, clinical audit, quality management) but NOT always for research.
- The HSE is not the data controller for personal/health data held in Section 38 acute hospitals which are legally independent organisations with respect to compliance with data protection legislation.
- The data controller for a research study is the organisation that determines the purpose and the manner by which personal data are processed **for the research study** (i.e. 'Whom', 'Why', 'How'). If the organisation takes these decisions with another organisation, they must specify the nature of their respective controllership (i.e. separate or joint controllers). Controllership is determined based on the factual elements and the circumstances of the research study, and the type of controllership determines the roles and responsibilities of the organisation.

29 Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) *OJ L 119, 4.5.2016, p. 1–88; https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32016R0679*

- For the purpose of this Framework, 'personal/health data' refers to any information, including sensitive information, (e.g. health, genetic, biometric), relating to an identified or identifiable individual, where the individual can be identified or is identifiable directly from the information in question, or indirectly from that information in combination with other information, (e.g. pseudonymised personal data remain personal data in the hands of the data controller).
- A PI employed by a healthcare delivery organisation (i.e. hospital, community or national services), acts as an employee of the data controller and is not, (in their own right), the data controller of personal data in patient records held by the organisation employing them. In such cases, the PI acts on behalf of the data controller and is responsible, along with the data controller, for ensuring compliance with GDPR and S. 36(2)(Health Research) of the Data Protection Act 201812 and subsequent amendments.
- When the data controller is the HSE, the relevant head or manager of a HSE site is responsible for ensuring data protection compliance within the site that they manage.
- In limited circumstances, it is possible for the PI to act as data controller if not acting as an employee of the HSE.[30]
- Where HSE staff hold a dual affiliation, they must decide which organisation (i.e. the HSE or the academic/other organisation) they will represent for the whole duration of the research study, and this determination must be done and confirmed in writing with the RGMS before the start of the research study. This is a vital requirement for the correct determination of controllership between the collaborative organisations.
- When the researcher is not a staff member of the research site, a research site responsible officer should be engaged to coordinate access to data for research purposes in an appropriate and legally compliant manner.
- Investigators should engage with their regional Deputy DPO for advice as required.

3.11 Data processor

A data processor is anyone who processes personal data on behalf of the data controller following strict instructions. Data processors should solely process data as requested by the data controller and must be a separate legal entity from the data controller. A processor becomes a controller if it does not follow the controller's instructions.

- When an employee of the HSE collaborates on a research study with a third-party, the HSE governance arrangements should ensure that such a situation is

30 For example, when the researcher acts in a private contractor capacity such as a GP.

appropriately registered. An appropriate determination of controllership must be done based the factual elements and the circumstances of the research study, to determine if the HSE (and the PI or researcher it employs acting on its behalf), acts as a controller or a processor for the purpose of the research study.[31]

- For the avoidance of doubt, an employee of the HSE cannot act as a data processor of personal data for the provision of health care.
- A data processor is defined as the organisation that processes personal data on behalf of, and under the instruction of, the data controller (i.e. two distinct organisations). Disclosure of personal data that is held by the HSE to a third-party is a processing operation, but such disclosure does not make the HSE a data processor.

3.12 Research governance, management and support functions

RGMS functions refers to the collection of activities that are required to provide institutional governance and oversight for research including registration, assessment of institutional risk, impact on the site, identity and insurance requirements, data protection compliance, contractual requirements, financial management and compliance with funder requirements.

Many of these activities currently take place in an uncoordinated manner and cause significant delays to project start up. The implementation of the framework will require the development of **Research Offices** at local, regional and national levels to coordinate these services and support staff to obtain the relevant approvals, as well as streamlined involvement of the relevant Data Protection officers for the host services when required (**i.e. the regional Deputy DPOs for HSE organisations**).[32] A proposed approach to the design of this function is outlined in Appendix 4.

3.13 HSE National Research and Development

HSE National Office for Research and Development will play a leading role in the development of the HSE national research policies, protocols, guidance and targeted training that need to be put in place to support the implementation of this Framework. The team will also support existing and future RGMS functions and RECs in developing their capacity to comply with this Framework. The office will also promote and support good practice in ensuring patients, carers, families, service users, and the public are involved in the planning, design, conduct, management, dissemination and translation of research.

31 E.g. in interventional research, information will be collected from participants and recorded in both the medical records for care purposes and in the Case Report Form or equivalent for research purposes on the instruction of a Third-Party. In this situation, the data is obtained **directly** from the participant and the Third-Party is the Controller for processing for research, with the hospital being a Processor acting in accordance with the instructions of the third-party for research purpose.

32 For HSE organisations, there is a Data Protection Officer (national) and four Deputy Data Protection Officers (regional).

4 Research approval, authorisation, oversight and management processes

Research as it pertains to this Framework (see Section 1.4 Scope), should be approved by both an appropriate REC and the relevant RGMS function before the research host site or service can authorise the commencement of the research activity. Equally, RECs and RGMS functions are also responsible for ensuring that **oversight, commensurate with the research study's risk and complexity**, exists for the duration of the project life cycle.

For the purpose of this Framework, 'pre-approval processes' refers to processes that take place before the research study commences, and 'post-approval processes' refers to processes of oversight taking place for the duration of the research study until project end.

4.1 Review, approval and oversight by the RECs

4.1.1 Review and approval by the REC

Research is essential for the continuous improvement of treatment, care and of health services, and for the prevention of ill health. However, research sometimes presents risks to participants. These risks, some of which may be known and some unknown, need to be assessed and considered in the context of the benefits of the research and minimised where possible. By ensuring that the research is carried out according to ethical principles, the process also protects the researcher and the organisation.

By ensuring that health research is underpinned by ethical principles, we comply with the principles of the Guideline for good clinical practice E6(R2),[33] promote public confidence in health research, and provide reassurance that the interests, dignity, welfare, rights and well-being of research participants are protected, and that their interests take precedence over those of science and society.

Research ethics review is the process whereby an appointed committee, composed of independent experts, generalists and lay people, **reviews a research study proposal and formally assesses whether the research is ethical. Based on this review, the committee may issue a favourable, unfavourable or conditional recommendation** (a favourable REC recommendation is hereinafter referred to as REC approval).

33 International Conference on Harmonisation/Good Clinical Practice (ICH GCP) guidelines European Medicines Agency. Guideline for good clinical practice E6(R2). London: European Medicines Agency; 2016. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-6-r2-guideline-good-clinical-practice-step-5_en.pdf

4.1.2 Principles underpinning research ethics review

A range of national and international guidelines on the conduct of ethical research has been published. These include: *The Nuremberg Code*,[34] the *Declaration of Helsinki*[35] and *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research.*[36]

Using international guidelines, Emanuel et al. proposed an ethical framework of seven principles, which provide coherent guidance to all clinical research stakeholders in all research settings. Reviewing research studies using these seven principles, (Value, Validity, Fair subject selection, Favourable risk–benefit ratio, Independent review, Respect for persons, and Informed consent) is the core business of the REC. A detailed description of these principles is included in Appendix 5.

4.1.3 Elements of the REC review processes

The REC reviews proposals in the context of the principles set out in Section 4.1.2 and evaluates the following elements for all proposed research studies:[37]

a) whether the health research is likely to assist in:
   (i) the advancement or protection of human health, whether of the population as a whole or of any part of the population,
   (ii) the scientific understanding of human health,
   (iii) the understanding of social factors affecting human health,
   (iv) the identification, prevention or treatment of illness, disease or other medical impairment,
   (v) the effective management of health services, including improvements in the delivery of those services.

b) whether the person making the proposal has identified and assessed the potential benefits and risks associated with carrying out the health research,

c) whether the person making the proposal will make every effort to ensure that the participation of individuals in the health research will be informed and voluntary,

d) whether the person making the proposal is qualified to carry out the health research concerned,

e) whether there are adequate safeguards in place to protect the privacy of individuals participating in the health research and the confidentiality of their personal data,[38]

34 The Nuremberg Code (1947). In: Mitscherlich A, Mielke F. Doctors of Infamy: The Story of the Nazi Medical Crimes. New York: Schuman; 1949: xxiii–xxv.
35 World Medical Association. WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects [Internet]. 2018 [cited Day Month Year]. Available from: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
36 The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. 1979. Available from: https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html
37 Source: Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018, Ireland. c2018. and 2020 Amendment.
38 This assessment may be done in collaboration with the data controller's data protection officer, if necessary.

f) whether there is anything in the health research concerned that will undermine or decrease public confidence in health research generally,

g) whether the research methodology proposed is appropriate,

h) whether any guidelines on ethical consideration issued by the HSE and/or NREC have been followed,

i) whether the proposed conditions in which personal and health-related data will be processed for scientific research are aligned with ethical principles,

j) whether the protocol for obtaining consent, the content of the participant information leaflet and of the consent form are aligned with data protection legislation, ethical principles and the National HSE Consent for Research Policy,[39]

k) whether patient, carer, service user and public involvement in the research process has been appropriately considered, and if so that it is ethical, legal and appropriately managed and supported.

l) The Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018 provides explicit consent as one of the required safeguards for the processing of personal data for health research. Explicit consent is informed consent that is duly recorded, and informed consent is a longstanding ethical requirement in health research. When obtaining explicit consent for the processing of personal data is not possible, a researcher can apply to the Health Research Consent Declaration Committee (www.hrcdc.ie) for a consent declaration to collect and use (but not disclose) personal data necessary for the research without the data subject's consent. A consent declaration will be given only where the researcher successfully makes the case that the public interest in the research significantly outweighs the public interest in obtaining consent.

4.1.4 Activities that do not require REC approval

Some research activities do not require approval from a REC. These include:

- research which exclusively involves the use of existing publicly available documents or data,
- case study reports of one participant, with the proviso that written informed consent has been obtained from the relevant study subject/participant.

39 The HSE National Consent Policy is under review at the time of publication of this Framework. As a result of this review process, a HSE National Consent Policy for research is currently under development as a separate policy and is due for publication in 2021.

Other activities involving analytical approaches and research methodology commonly take place as part of service planning or quality improvement, but they are regulated by different governance processes, (i.e. the health research regulations do not apply, but other governance mechanisms do apply). These include:

- clinical audits,
- standard service evaluation and development,
- health surveillance,
- normal and statutory public health work,
- advanced health analytics carried out by the service for the purpose of service planning or quality improvement.

4.1.5 Follow-up of ongoing research studies by the REC

Ongoing research studies should be subject to continued ethics oversight. The frequency of such reviews should reflect the degree of risk to participants in the research study. This may involve review of regular safety reports and of any relevant interim or close-out reports (see "Tracking of the Research Study" in Section 4.2.3).

Any significant alteration to a previously approved proposal must receive prior approval from the REC before implementation. Such alterations would include changes in personnel, methods, design, duration, informed consent procedures, patient information sheets, or methods of recruitment.

Investigators must immediately report Suspected Unexpected Serious Adverse Reaction (SUSARs) to the Sponsor and REC. Investigators must immediately report any serious or unexpected adverse events occurring in participants, or any unforeseen events that might affect the risk–benefit ratio of the proposal, to the REC. For example, they should report any untoward medical occurrence that results in death, is life threatening, or requires in-patient hospitalisation [under S.I. No. 878/2004 – European Communities (Clinical Trials on Medicinal Products For Human Use) (Amendment) Regulations 2004, a written report of any urgent safety measures taken should be submitted to the REC no later than 3 days from the date the measures were taken].

In the case of a premature suspension/termination of a research study, the REC should require the investigator to inform the REC of the reasons for premature suspension/termination. This should be accompanied by a summary of the results obtained in the study up to the point of suspension/termination.

4.1.6 Remit of the NREC versus local RECs

The mission of the National Office for Research Ethics Committees is to embed a robust, transparent and cohesive research ethics review system that strengthens the national research infrastructure. The National Office for Research Ethics Committees will establish NRECs in prescribed areas of health research at the request of the Minister for Health. While NRECs will be established in a variety of health research areas over time, the initial priorities of national strategic importance are for CTIMPs and clinical investigations of medical devices.

An essential aspect of the NREC system is the mandate to return ethics decisions that are respected nationally ('single national ethics opinion'). This will enable the NREC review process to run in coordination with the HPRA, where necessary, in order to ensure that Ireland meets its member state obligations to return a 'single national ethics opinion' in relation to pending EU regulations, including for CTIMPs (Clinical trials – Regulation (EU) No 536/2014) and clinical investigations of medical devices (Regulation (EU) No 2017/745). The remits of the NREC-CT and NREC-MD will be based on these EU regulations. All other health research studies as described in Section 1.4 (Scope) must be approved by a HSE REC, hospital REC or HSE-approved REC.

Working alongside local RECs and supported by the National Office for Research Ethics Committees, the NRECs will work in a mixed-model system to support research ethics across the spectrum of health research in Ireland. An essential requirement for the cohesion of this mixed-model system is clarity of committee remits at local and national levels. In this regard, following a defined period of transition, local RECs will not be authorised to review research studies that fall within the remit of the NRECs. The research community, including local RECs, will be expected to respect the outcomes from the NREC process. At a practical level, this means a research organisation should not require a researcher to secure local ethics approval in addition to NREC approval, nor should a local REC re-examine an NREC decision. Correspondingly, an NREC will not revisit a decision made by a local REC within its local remit. It is important to note that NREC approval will be contingent on the necessary governance approvals being in place locally to conduct the research at the sites proposed.

While the local RECs and NRECs will have distinct remits, the effectiveness of the mixed-model system will rely on appropriate communication channels between both, in order to ensure that the entirety of Irish health research is grounded in the highest standards of ethics, governance and research practice.

4.2 Review, approval and oversight by the RGMS function

4.2.1 Review and approval by the RGMS function

RGMS function review refers to the process whereby a research study hosted by a health and social care organisation can be assessed and recommended for approval before the research study commences. This review would be in addition to, and could be done in parallel with, a REC review. Healthcare providers are responsible for the research that takes place on their premises, is conducted by their staff, and/or involves their service users.

The objective of this assessment is to:

- ensure that the service provider has visibility and full knowledge of the research conducted by its staff, or that involves patients and/or the service provider's staff,
- determine the organisational **risk** and ensure that proportionate study governance is in place for the research study,
- ensure **compliance** with regulatory (HPRA regulations), legal (i.e. data protection), financial (i.e. financial regulations of EU research funding) and professional standards, as well as organisational policies and standard operating procedures,
- ensure that the **responsibilities** of all parties related to the research study have been identified and appropriately allocated before the research study commences,
- ensure that appropriate **insurance** arrangements and a **contractual framework** are in place before the research study commences,
- assess the suitability of arrangements for the **financial, intellectual property and human resources management** of the research study. Operational arrangements may be delegated to, or done in collaboration with, third-level institutions when appropriate.

RGMS function review involves the **registration of a research proposal to enable the formal assessment of all of the above aspects. Based on this assessment, a favourable or unfavourable recommendation will be issued** by the RGMS.

4.2.2 Principles underpinning RGMS approval of research studies

The following principles underpin the process of organisational review of research studies:

- All proposed research studies should be registered, reviewed and approved before commencement. This applies to **all health research** studies regardless of the level of patient intervention.

- Registration should be enabled by way of a standard application form and the process should be coordinated with the REC submission, as well as third-level institution approval and/or approval from other regulatory bodies, in order to avoid delays and duplication.
- The extent of the RGMS function review needs to be **proportionate** to the organisational risk (e.g. legal, financial) and the impact on the provision of health and social care services.
- All clinical trials must have a **clearly identified sponsor who takes overall responsibility for the study.**
- Sponsors should give consideration to the appropriate and effective inclusion of patients, carers, service users, and the public in the study planning, design, conduct, management, dissemination and translation of research findings.
- The responsibilities of the legal entity or each of the legal entities responsible for a research study that is not a clinical trial or intervention must be articulated before the research study starts.
- For research studies involving staff with **joint clinical/third-level institution appointments**, the employing organisation carrying responsibility for the study must be disclosed and approved and in the case of joint responsibility, both employers should review and approve the research study (e.g., joint review and approval processes may be put in place when appropriate).
- PIs or relevant parties should be given the opportunity to address any concerns that may arise during the assessment process and provided with relevant support to address them.

4.2.3 Ongoing oversight by the RGMS function

Once the research study commences, ongoing oversight processes should be in place to provide quality control, management and governance assurance to the service hosting the research.

The level and frequency of oversight for each research study should be determined by the **assessment of organisational risk prior to approval**. Ongoing oversight may include monitoring (if appropriate), tracking and audit processes. In addition, the RGMS function has an important role to play in cases of research misconduct.

Monitoring of the research study

Monitoring is a quality control function where research study conduct is routinely assessed on an ongoing basis at every step of the clinical trial:[40]

- Monitoring is carried out in order to ensure that the sponsor's responsibilities are being met, and in particular, that:
  - the rights and well-being of participants and those who are patient partners in the conduct and management of a research study are protected,
  - the research study data are accurate, complete and verifiable,
  - the research study complies with regulatory processes and guidance (for regulated research studies),
  - processes are taking place in line with agreed protocols.
- Monitoring is the responsibility of the sponsor organisation and takes place during the research study conduct phase.
- The sponsor may employ their own monitor, or delegate the monitoring role to a contract research organisation (CRO) or to a CRF/C. This delegation should be formally documented.
- Not all studies require monitoring: it is a mandatory requirement for CTIMPs and clinical investigations, but may also be deemed necessary for other research studies by the sponsor and/or the RGMS function, in order to mitigate risk.
- Commercial research studies sponsored by a company are usually monitored by external monitors that come onsite as required by the study.
- Medium to high-risk, non-commercial research studies sponsored by third-level institutions, hospitals or other non-commercial organisations may put in place monitoring arrangements via the relevant CRFs, other organisational CRCs or external CROs.
- Responsibilities delegated to the CRF, CRC, CRO or other parties should be appropriately documented for all studies.

Tracking of the research study

Tracking is a process whereby simple pro-forma reports are submitted by the PI to the RGMS function at agreed intervals and at research study close in order to check whether the study is progressing or has been completed according to the original plan. Such reporting is the responsibility of the PI.

- The managing of interim and final reports is the responsibility of the RGMS function acting on behalf of the hospital or relevant service and on behalf of the relevant REC.

40 Monitoring is used by sponsors of clinical trials to oversee the conduct of, and reporting of data from clinical investigations, including appropriate supervision of research study site staff and third-party contractors. Monitoring activities include communication with the research study site staff; review of the research study site's processes, procedures, and records; and verification of the accuracy of data submitted to the sponsor.

- The final or close-out reports should then be submitted to the relevant REC (to fulfil the research study follow-up requirements for RECs, as described in Section 4.1.5.) and also to the management team in the relevant service. In situations where the research activity is very high, reports to the management team could be submitted on an annual basis, or as agreed. Management reporting is necessary in order to increase awareness and maximise the potential for knowledge translation.
- Tracking enables the gathering of up-to-date information about all registered research studies, i.e. current, active and closed studies. It also enables the management team to have oversight of the number of participants enrolled in the research studies hosted within their site(s).

Audit of the research study by the RGMS

A research study audit is a quality assurance activity to provide an independent check that a research study is being conducted in accordance with the protocol, the principles of good clinical practice (where appropriate), and the terms of the REC and regulatory authority approvals for the study. Study audits may be carried out on an annual basis on a small sample of research studies, and they may involve an independent, systematic evaluation of processes and quality control.

- Research study audits are the responsibility of the RGMS function acting on behalf of the hospital or relevant service.
- Research study audits check whether the study is being conducted in compliance with local quality management systems, GCP, and all applicable legislative, regulatory and local requirements.
- Research study audits are carried out by the RGMS function in the host site or service and such audits should be proportionate to the level of risk associated with the study.

Dealing with fraud and misconduct

Fraud and misconduct in research[41] are rare, but it is a serious issue when it occurs. During the course of a research study, individuals may report suspicion of fraud or misconduct to the RGMS function or to the REC. Alternatively, it may be identified during an audit process. In such cases, an investigation will be required to assess whether any non-compliance issues are a result of misconduct or fraud.

Employers are responsible for ensuring that the principles of research integrity outlined in the *National policy statement on Ensuring Research Integrity in Ireland*[42] are followed by their staff. They will act to deal with suspected fraud or misconduct in accordance with their standard operating procedures and human resources policies and procedures. When the PI has a joint appointment with a healthcare service provider and a third-level institution, the responsibilities of each in relation to dealing with research misconduct should be agreed in advance of commencement of the research study.

4.3 Authorisation by the relevant health or social care service provider (the research site)

The assessment by both the REC and the RGMS function provides the basis for a recommendation to the relevant health or social care service provider hosting the research, who then has the final authority to either grant or not grant approval.

REC and RGMS approval (and, where necessary, regulatory approval) of research is required before a research study can be given site authorisation to commence. The host site or relevant service provider ultimately retains the authority to decide not to commence the research study, even with a positive recommendation from the REC and the RGMS function.

41 For further guidance and information, see the National policy statement on Ensuring Research Integrity in Ireland (2014) at http://www.iua.ie/wp-content/uploads/2014/06/National-Policy-Statement-on-Ensuring-Research-Integrity-in-Ireland-2014.pdf and the OECDOECD's at: http://www.oecd.org/sti/scienceandtechnologypolicy/40188303.pdf. Best Practices for Ensuring Scientific Integrity and Preventing Misconduct at http://www.oecd.org/sti/scienceandtechnologypolicy/40188303.pdf.

Fraud and misconduct in research involveinvolves:

- fabrication
- falsification
- misrepresentation of data and/or interests and/or involvement
- plagiarism
- failures to follow accepted procedures or to exercise due care in carrying out responsibilities for:
    - avoiding unreasonable risk or harm to:
        - humans
        - animals used in research
        - the environment.
    - the proper handling of privileged or private information on individuals collected during the research study.

For the avoidance of doubt, misconduct in research includes acts of omission as well as acts of commission. In addition, the standards by which allegations of misconduct in research should be judged should be those prevailing in the country in question and at the date that the behaviour under investigation took place (UK Research Integrity Office 2017).

42 Irish Universities Association. National policy statement on Ensuring Research Integrity in Ireland (2014).. Dublin: Irish Universities Association; 2014. Available from: https://www.iua.ie/wp-content/uploads/2019/09/National-Policy-Statement-on-Ensuring-Research-Integrity-in-Ireland-2014-1.pdf

The implementation of the national research information management system will enable an efficient and effective process for both ethical and governance review and approval.

4.4 Post-approval management by the PI of health research studies

The management of health research studies (see Glossary of key terms) is the responsibility of the PI, who may be supported by services provided by CRFs or CROs (often clinical discipline specific, with a relevant track record and critical mass), oncology clinical trial units, third-level institution departments or other entities. The elements listed below may be required depending on the research study.

Quality management systems
A quality management system should be in place to assess and manage risk for the duration of the research study and provide assurance of quality and safety.

Management of research study files: documentation, filing, storage and archiving
Assurances may be required that research study files and documents are being stored securely and safely according to data protection legislation and the standard operating procedures of the host site/HSE in relation to information governance and management of documentation.

Research data should be retained for 5 years (as per the National policy statement on Ensuring Research Integrity), or longer if necessary, in order to comply with legal requirements (i.e. clinical trials legislation) or additional local policies for the retention of data and to enable evaluation of the study processes. Archiving arrangements must be agreed between the sponsor/responsible legal entity and the host site, and appropriately documented.

Data management processes
Research study data should be accurate and complete, and should comply with the protocol, GCP (when appropriate) and regulations.

Financial management
The financial aspects of the research study must be managed appropriately, so that the study is not adversely affected. Financial information on the research study should be provided to the relevant RGMS function, as required.

Safety and adverse events
Investigators must report serious or unexpected adverse events occurring in participants, or unforeseen events that might affect the risk–benefit profile of the research study. The Sponsor is responsible for identifying, documenting and reporting

all suspected unexpected serious adverse reactions (SUSARs) to the HPRA and the REC, as required. It is recommended that the HSE Integrated Risk Management Policy: Incorporating an overview of the Risk Management process[43] is adhered to and all investigators comply with the HSE Incident Management Framework 2020,[44] if an adverse event/reaction occurs, and that this incident reporting system also be used to inform the REC and the RGMS function.

All incidents, as per clinical best practice, must be reported via the National Incident Management System (NIMS), which the relevant DSA will have access to.

Research study closure

The PI is responsible for maintaining up-to-date records of a research study closure or ending on behalf of the host site. The PI (or chief investigator for multisite studies) should notify the RGMS that the research study has ended, whether this is a planned closure or because of early termination. If the research study has terminated early, the reasons should be documented. A final report should be submitted to the RGMS function and to the REC.

Research dissemination

Unless the REC agrees otherwise, it is best to communicate the research results to those who consented to be involved in a research study (including the relatives of deceased patients who have agreed to the use of organs or tissue in the research). Specific approaches may need to be used in order to ensure that research findings are accessible to participants and/or the relatives of deceased patients, and this may involve using different media and writing styles for different audiences. Where patient, carer, service user, public partners have been involved as co-researchers or members of the research team, it its good practice they should be involved in the dissemination process.

Clinical trial registration

In line with the 2013 *Declaration of Helsinki and the HRB's Clinical Trials and Interventions Research Governance Policy*, all clinical trials and interventions should be registered in a publicly available, free-to-access, searchable clinical trial or investigation registry, or database where available, prior to initiation of the research study.

Examples of clinical trial or investigation registries include ClinicalTrials.gov, the ISRCTN Registry, the EU Clinical Trials Register, or any another register listed on the World Health Organisation's International Clinical Trials Registry Platform.

43 Health Service Executive. HSE Integrated Risk Management Policy: Incorporating an overview of the Risk Management process. Dublin: Health Service Executive; 2017. Available from: https://www.hse.ie/eng/about/qavd/riskmanagement/risk-management-documentation/hse%20integrated%20risk%20management%20policy%202017.pdf

44 https://www.hse.ie/eng/about/qavd/incident-management/hse-2020-incident-management-framework-guidance.pdf

5 Framework implementation and compliance

By its nature, research is collaborative and often involves multiple sites and third-level institution partners. It is therefore important that a national unified approach is adopted for the implementation of this Framework, in order to facilitate rather than hinder research. The development of standalone individual approaches will inevitably result in a fragmented system that will only exacerbate existing problems, and the National Research Oversight and Governance Board[45] will have a key role in ensuring that the implementation of the necessary structures results in an efficient and integrated national system[46]. Furthermore, RGMS requires significant resources that may not be readily available to all services. Therefore, the development of structures that can provide research management capability and support to multiple sites, as well as provide a collaborative approach to third-level institutions that have already developed research governance systems, is highly recommended.

Notwithstanding the Sláintecare plans to evolve towards integrated models of care underpinned by different regional structures, the current existence of the HGs and the existence of the HSE National Office for Research and Development provides an opportunity to commence the implementation of new governance arrangements for research that can evolve to suit the needs of integrated care organisations in due course. The HGs are associated with third-level institutions that have been key partners in the development of clinical research since around 2010. The role of the chief academic officer and the development of academic health centres are also essential developments in this context as precursors of future or academic health systems, which incorporate community services. Consequently, it makes sense to commence the implementation roadmap for this HSE Framework for the Governance, Management and Support of Research at the level of the HGs by capitalising on existing structures, linkages with third-level institution partners and historical integrated work already underway, with a view to evolve research governance and management structures to community-based research in the near future.

Both the HSE Research Governance, Management and Support Framework Implementation Working Group and the REC Reform Working Group were established in 2020 with a view to developing a consensus approach to the implementation of this Framework and the reform of the HSE Research Ethics Committee system. The aim

45 The National Research Oversight and Governance Board will have key representatives from HSE and S38 organisations as well as two patient representatives from the national R&D PPI Advisory Group.

46 See Appendix 4 for further information on the structures required to implement the research governance, support and management functions required for the implementation of this Framework, including the role of the National Research Oversight and Governance Board.

is to develop an integrated system and to avoid the development of individual local approaches, which may hinder collaborative research rather than support it.

The implementation of this Framework will be informed by previous work conducted by the Corporate Enabling of Clinical Research initiative and supported by further development of national HSE research-related policies and guidance to facilitate the process of research across organisations, and to support transparent, safe and high-quality research in order to guarantee public confidence. Senior management of healthcare organisations engaged in research activity are responsible for ensuring that research governance arrangements aligned to this framework are put in place. The National Research Governance and Oversight board working with the HSE National Office for Research and Development will have an important role in monitoring the implementation of this framework going forward. HSE Internal Audit[47] and the HSE Audit and Risk Committee[48] will have respective roles in assuring and overseeing compliance with this framework.

47 HSE Internal Audit provides an independent, objective assurance and consulting activity designed to add value and improve an organisation's operations. It helps an organisation accomplish its objectives by bringing a systematic, disciplined approach to evaluate and improve the effectiveness of risk management, control, and governance processes.

48 The Audit & Risk Committee is a subcommittee of the HSE Board. Under legislation, this committee advises the HSE Board and the HSE Chief Executive on a variety of matters including advising on the appropriateness, effectiveness and efficiency of the HSE's procedures relating to, inter-alia, risk management and internal audits.

Appendix 1

Working Group for the Development of the HSE Framework for the Governance, Management and Support of Research

The development of this Framework has been led by the HSE National Office for Research and Development (R&D), with the support of a working group of key stakeholders. The members of the group include:

- Dr Ana Terrés, HSE Assistant National Director, Head of Research and Evidence (Chair)
- Dr Natalie Cole, Senior Research and Development Manager (Project Manager)
- Dr Virginia Minogue, former research lead for NHS England and Executive Group member of the NHS Research Forum
- Prof. Helen Whelton, Chief Academic Officer of the South/Southwest Hospital Group
- Dr Anthony O'Regan, Chief Academic Officer of the Saolta Hospital Group
- Prof. Tim Lynch, Chief Academic Officer of the Ireland East Hospital Group
- Prof. Paul Burke, Chief Academic Officer of the University of Limerick Hospital Group
- Prof. Owen Smith, Chief Academic Officer of Children's Health Ireland
- Dr Karn Cliffe, Nominated Representative of the Dublin Midlands Hospital Group
- Dr Séamus Browne, Head of Industry Partnerships, Royal College of Surgeons in Ireland (RCSI) – representing the RCSI Hospital Group
- Dr Una Fallon, Consultant in Public Health Medicine and Chair of the HSE Midlands Research Ethics Committee
- Ms Carol Ivory on behalf of HSE Acute Operations
- Mr Gareth Davies on behalf of HSE Community Operations
- Ms Sandra Daly, Chief Executive Officer, Mercy University Hospital
- Dr Mairéad O'Driscoll, Chief Executive Officer, HRB
- Dr Anne Cody, Head of Pre-Award, HRB

HSE National Office for Research and Development (R&D)

- Dr Ana Terrés, HSE Assistant National Director, Head of Research and Evidence
- Dr Natalie Cole, Senior Research and Development Manager
- Dr Declan O'Hanlon, General Manager, HSE R&D
- Ms Laure Méchineau-Phelan, Senior Manager Contracts and Data Governance

Advisory Groups

- HSE REC Reform Working Group
- HSE Governance Implementation Working Group
- HSE National R&D PPIU Advisory Group.

Appendix 2

Roles and responsibilities within the research governance cycle

Further details on the roles and responsibilities of certain key stakeholders within the research governance cycle are included below. A comprehensive list of roles and responsibilities can also be found in the ICH GCP Guideline.[49]

Responsible legal entity for clinical trials

The responsible legal entity for clinical trials and interventions is called a sponsor. For all other research studies, the legal, financial and other responsibilities may be distributed among several legal entities.

49 https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf

Sponsor

Pre-approval responsibilities	Post-approval responsibilities

The sponsor is responsible for:
• The initiation, management and/or financing of clinical trials and interventions, but not for actually conducting the investigation.
• Ensuring that the investigator, research team and site are suitable and that roles and responsibilities are clear.
• Ensuring appropriate use of patient, service user and public involvement.
• Ensuring that arrangements are in place for the research team to have access to resources and support in order to deliver the research as proposed.
• Allocating responsibilities for management, monitoring and reporting of the research.
• Ensuring that provision has been made for the adequate insurance and indemnity, which may arise in relation to the study. (The extent and limitations, if any, of insurance cover should be adequately communicated to participants of the study).
• Identifying the associated risks and appropriate mitigating actions with the support of the principal investigator.
• Ensuring that proposals and protocols have ethical approval.
• Ensuring that data management arrangements are appropriate.
• Ensuring compliance with legislation and with contractual obligations.
• Giving the green light for research studies to commence once satisfied that all relevant governance is in place.
• Ensure patient, carer, service user, public partners have access to appropriate and relevant training and support.
• Ensuring appropriate checks have been undertaken on suitability for PPI involvement.
	• Ensures that appropriate monitoring arrangements are in place for all clinical trials and interventions.
	• Ensures that the distribution of delegated tasks is clearly documented and agreed throughout the lifespan of the research study, and that each party has the control and access to data and information that their legal responsibilities require.
	• Ensures that:
	  • the conduct of the research study is compliant with relevant legislation.
	  • the rights and well-being of participants are protected.
	  • the research study data are accurate, complete and verifiable.
	  • the research study complies with appropriate regulatory processes and guidance.
	  • processes are taking place in line with agreed protocols.
	• Ensures that substantive changes to the protocol/proposal are submitted for ethical review.
	• Ensures that serious and adverse events are reported to the REC, SCA, and any relevant regulatory bodies.

Principal investigator

Pre-approval responsibilities	Post-approval responsibilities
• It is the responsibility of the PI of the research study to be aware of and adhere to the procedures outlined in this Framework. • The PI develops proposals that are scientifically sound and ethical. • The PI ensures that arrangements are in place (i.e. delegates responsibility to appropriate CRF, CRC, CRO) to enable the PI to discharge their responsibilities and, if required, identifies the sponsor of investigator-led clinical trials or interventions. • The PI works with the sponsor in the preparation of the risk assessment for the proposed research study. • The PI ensures that the research study has been submitted for approval to the R&D office and that the information in the application form is accurate. • The PI obtains approval for the research study from their line manager prior to submission for approval to the REC and to R&D office. It is the responsibility of the PI to obtain permission to carry out the research study from the relevant HSE manager. • The PI ensures that the research study is submitted for independent ethical review. • The PI should not start the research study until REC authorisation and site authorisation is obtained. • The PI ensures that they have adequate insurance and indemnity for their research activity upon commencement. • The PI assesses the data protection-related risk, and prepares a data protection impact assessment for the research study if required. • Where appropriate involves patient, carer, service user, public partners in the study planning, design, conduct, management, dissemination and translation of research findings. • Ensures agreements are in place with PPI contributors.	• Ensures that research is carried out according to the terms approved by the REC and the R&D office (unless urgent safety measures are necessary). • Ensures that each member of the research team, including those at collaborating sites, is qualified by education, training and experience to carry out their role in the research study. • Ensures that reports on the progress and outcomes of the work (i.e. to the sponsor, funders, regional and HSE National Office for R&D or others with a legitimate interest) are produced on time and to an acceptable standard. • Reports any complaints, allegations of research misconduct, or conflicts of interest to the REC and R&D office as appropriate. • Ensures that substantive changes to the protocol/proposal are submitted for ethical review and for review by the R&D office. • Ensures that serious and adverse events are reported to the sponsor and the R&D office. • Reports all incidents relating to clinical trials and interventions to the SCA. This must be done via the National Incident Management System (NIMS), which the relevant delegated State authority (DSA) will have access to. • Completes the requirements for closure of the research study and submission of the end of study report to the R&D office and the REC. • Ensures adherence to Data Protection legislation throughout. • Ensures the wellbeing and support of patient partners for the duration of their involvement.

Research site

Role	Pre-approval responsibilities	Post-approval responsibilities
The PI's line manager or head of service, as appropriate	• Ensures that the site has the capacity to host a research study and that the impact of the study on the site is acceptable, as appropriate. • Ensures that the staff member has the capacity and is given the time to participate in the research study, as appropriate.	• Engages with the PI, should any issues arise that may affect the research site's capacity to host the study. • Reports to the R&D office and, where applicable, to the sponsor, any concerns related to any ongoing studies being led by the PI.
CRF or CRC director	• For those research studies using CRF/C facilities, ensures that the CRF/C has the capacity to provide the necessary support and sign-off on the study. • Signs off on any contractual agreement with the research sites and/or the third-level institution and/or commercial sponsor that articulates the level of service provided to a particular research study.	• Ensures that the service provided by the CRF for the sponsor (i.e. third-level institution, PI), is of the standard required.
Organisation's authorising officer (e.g. hospital Chief Executive Officer/Community Healthcare Organisation Chief Officer), or their delegated authority	• Authorises the commencement of a research study at their site. • This includes all studies taking place in academic CRFs or CRCs that involve service users. • It is best practice that this authorising officer (or delegated authority) is not a member of the REC that approved the research study.	• Has overall awareness of the research activity taking place within the site. • Provides leadership and has a key role in the development of a research culture within the site.
Research site responsible officer (for external studies)	• Responsibilities may vary depending on the type of research study and the type of involvement. • At a minimum, this is the person who coordinates and facilitates access to the site or data in a manner compliant with this Framework, as well as with relevant HSE policies and legislation.	• Provides general oversight of activities by researchers external to the site. • Ensures termination of access upon research study completion.

Research governance, management and support (RGMS)[50] function

Pre-approval responsibilities	Post-approval responsibilities
• Manages the administrative aspects of registration and approval of research studies. • Reviews the submitted research application form and determines whether the research study is low, medium or high risk. • If appropriate, expedites the assessment of low-risk research studies and recommends approval to a host site for sign-off by the appropriate authorised representative. • Obtains advice on medium and high-risk research studies from research management roles that have expertise in the area (e.g. legal, data protection, or financial expertise may be required). • Ensures evidence of an independent ethical review before recommendation of approval to a host research site. • Reviews the research application form, risk assessment, and data protection impact assessment (DPIA) (if applicable) to determine the level of risk of the research study. • Reviews insurance and indemnity arrangements including cover for any patient partners • Provides a recommendation to the research site for sign-off or rejection by a designated authority.	• Provides appropriate reports and metrics for management purposes (local, regional, national). • Keeps all documentation relating to the process of approval of research studies in a secure manner. • Tracks the compliance of the research study with the approved application through review of progress reports submitted by the PI. • Tracks any special conditions imposed on the conduct of research. • Reviews reports from independent agencies (e.g. HPRA, HRB) concerning the research study. • Conducts or coordinates audits of research studies in research sites, where required. • Reviews or manages amendment documentation related to approved research studies that have implications for the host site. • Processes complaints relating to the conduct of the research study. • Reviews adverse event reports and serious adverse event reporting. • Escalates issues if the research study is not compliant with original approval and protocol. • Completes requirements for research study closure. • Receives and manages the investigation of allegations of research misconduct. • Reviews required reports, and receives and investigates conflict of interest allegations.

50 The RGMS function may incorporate a number of elements according to specific needs; hence, some of these functions may be divided among the different components of this function (see Appendix 4).

Research Ethics Committee

Pre-approval responsibilities	Post-approval responsibilities
• Performs ethical assessment of the risks to the participants, consent procedures, and scientific importance. • Assesses the ethical aspects related to data protection and confidentiality. • Ensures that methodology is ethically sound and of good quality. • Ensures that all steps of the research process follow ethical standards throughout the research study life cycle (consent, patient information sheets). • Provides feedback to the applicant on the outcome of the ethics review. • Provides advice when a consent declaration / application to the Health Research Consent Declaration Committee is required.	• Considers and validates amendments to study protocols of previously reviewed research studies. • Receives annual reports on the progress of research studies it has reviewed. • Receives a final report on research study closure. • Performs regular ethical reviews of ongoing research studies. • Reviews and advises on reports of serious or unexpected adverse events occurring in participants or unforeseen events that might affect the risk–benefit ratio of the proposal. • Reviews reports in cases of a premature suspension/termination of a research study, and requests an investigation if necessary. • Archives REC documentation, including written REC standard operating procedures, annual reports, CVs of each REC member, records of all income and expenditure, meeting agendas and minutes, correspondence to applicants, and final research study reports.

Health Products Regulatory Authority (HPRA)

Pre-approval responsibilities	Post-approval responsibilities
• Reviews and approves clinical trial applications. The ethics committee submission can be made before, in parallel with, or after the HPRA application. • Checks that the sponsor or legal representative of the sponsor is based in the EU or European Economic Area (EEA). • Provides status updates (authorised, rejected, withdrawn) on reviewed clinical trials to EU clinical trials register (EudraCT). • Ensures that REC approval has been granted prior to issuing HPRA approval.	• Receives notification of urgent safety restrictions from the sponsor. • Receives annual reports on the progress of approved clinical trials, including safety data. • Receives end of trial declarations. • Receives reports on any serious adverse reactions and untoward incidents. • Takes actions that may be necessary in case of concerns regarding subject safety or scientific validity of a clinical trial, including halt to recruitment, suspension or prohibition of conduct. • Undertakes good clinical practice (GCP) inspections of investigator sites, clinical trial hosts (e.g. CRFs) and sponsors to establish whether the conditions and principles of GCP are satisfied or adhered to in relation to clinical trials. Inspections may also be conducted prior to clinical trial approval where required. Entities are selected for inspection using a risk-based approach.

Appendix 3

HSE Research Ethics Committee reform roadmap: a summary

The current REC landscape in the HSE is fragmented and uncoordinated. Historically, RECs were set up to address the needs of individual hospitals or to address the needs of the various organisations within regional health boards. The creation of the Community Healthcare Organisations and the Hospital Groups (HGs) was not accompanied by a restructuring of the REC system in the HSE, and the current structure causes significant challenges for both researchers and clinical trial sponsors alike.

Both the establishment of the National Research Ethics Committee (NREC) by the Department of Health and the development of new governance structures for research require the urgent reform of the HSE research ethics committee system if research is to be facilitated rather than hindered.

There are at least 32 RECs associated with the HSE and with Section 38 and 39 organisations. The proposed reform will require the creation of seven HSE Reference RECs (six aligned to each of the future Regional Health Areas and one aligned to Children's Health Ireland) which will operate to high operational and transparency standards and will be supported by a central national coordinating office. These HSE Reference RECs will work with the NREC and RECs within individual organisations to contribute to an integrated national system.

All HSE Reference RECs will:

- have standardised approaches to REC protocols and management,
- report to a suitable governance structure within the HSE,
- have processes integrated with the local RGMS functions in their area,
- be supported by the national or local Research and Development offices (i.e. recruitment, training opportunities and induction for members),
- have an appropriate financial and sustainability model,
- provide full national coverage for all HSE organisations within their area, as well as for HSE organisations that are funded by the HSE but have no REC (i.e. Section 38 and 39 organisations),
- recognise each other's approvals,
- have appropriate patient and public representation in their membership.

Appendix 4

The HSE Research Governance, Management and Support (RGMS) function

The RGMS function is an essential requirement to provide appropriate governance for research activity at local level. This function may be structured differently in different parts of the service, but key components may include the following:

Research and Development Offices (i.e. HSE National Office for R&D, Hospital Group R&D offices, or in the future, Regional Health Area R&D offices). This is the core administrative and coordinating office for all the research activity in a given jurisdiction or service. It manages the registration of proposals and coordinates the technical review and risk assessment of the research studies. It liaises with the Research Governance Board (see below) and provides research support or oversight structures at local level. This office coordinates the submission of approval to authorise the research study to the research site.

These offices will play a key role in the implementation of this Framework.

Research management roles: These include a number of roles with key technical expertise specific to research activity, including:

a. risk assessment
b. data protection and data management
c. legal and contractual matters
d. regulatory and quality affairs
e. research finance
f. intellectual property
g. human resources management
h. research support, including supporting staff with their PPI plans.

Some of these roles may be appointed in collaboration with third-level institution partners (hence becoming key enablers of the Academic Health Science System model), may be part of local R&D offices, or may leverage from existing roles and structures within the health and social care provider organisations.

The primary role of a **Data Protection Officer (DPO)**[51] is to assist their organisation in all issues relating to the processing of personal data. In particular, the DPO / regional Deputy DPOs must:

- Inform and advise their organisation and its employees of their obligations under data protection law, including advising on interpretation or application of legislation,
- Ensure relevant individuals are informed about their data protection rights, and act as a contact point for requests from individuals regarding the processing of their personal data and the exercise of their rights,
- Monitor compliance of the organisation with all legislation in relation to data protection, including audit,
- Awareness raising activities, as well as training of staff involved in data processing,
- Provide advice on DPIAs, review DPIAs and monitor their performance,
- Provide advice on relevant agreements (e.g. data sharing agreements),
- Cooperate with the Data Protection Commission (DPC) and act as a contact point on issues relating to processing,
- Handle incidents and breaches and provide required advice on notifications and communication.

Researchers should engage with their regional Deputy DPO in a timely manner if the research study risk in relation to data protection warrants it.

The DPO is an independent figure who must not receive any instructions from the organisation regarding the performance of their tasks. The DPO reports directly to the highest level of management of the organisation.

Research support officers or coordinators: These roles provide a liaison and coordinating role between a research site (i.e. a hospital or a community service) and the regional R&D office of their jurisdiction, and provide support to the staff within the research site.

Local research committee: (i.e. in individual hospitals or community services). These committees are required at a minimum for those hospitals or community sites that take on the role of the sponsor of clinical trials for medicinal products or clinical investigations with medical devices. While the relevant R&D office and the research management roles will perform the due diligence with respect to the risk and other technical aspects of the research study, it is the decision of the local research committee to assess the recommendation provided by the research office and accept the role of sponsor of a clinical trial. This committee may have additional

51 Note that in the HSE, the role of the DPO is discharged by the DPO and the regional Deputy DPOs.

responsibilities as required by the local site such as, overseeing all research activity; making decisions related to research investments; supporting the hospital or site in developing funding and income streams; supporting the development of existing and emerging research partnerships; reviewing the volume, type and impact of research activities undertaken within the site; and reviewing and advising the management board on research policies and procedures. These committees could also play a role in fostering and encouraging inclusion of PPI in research in their sites.

Regional Research Governance Board: This provides overall governance and strategic direction for the research activity of the relevant jurisdiction (i.e. Regional Health Areas), and it should have relevant representation from third-level institution partners as well as PPI, when appropriate.

Clinical Research Facilities or Centres (CRF/Cs): CRF/Cs provide the infrastructure, the physical space and facilities, the experienced research and specialist support staff, and the necessary quality and oversight programmes that are critical for the successful conduct of patient-focused research.

The overall implementation of this Framework will require the establishment of a HSE **National Research Oversight and Governance Board**, led by the HSE and comprising an appropriate cross-section of key stakeholders, including PPI, which will support integrated oversight and monitoring across Hospital Groups, CHOs as well as external/internal partners and will revolve around three National Project Pillars:

Pillar One: The reform of the existing Research Ethics Committee system in line with international standards.

Pillar Two: The establishment of new functions for research governance, management and support at local, regional and national levels.

Pillar Three: Procurement and roll out of the Electronic Research Information Management System (ERMS) to enable an integrated approach to ethics and RGMS approval protocols and to facilitate collaboration between organisations.

Appendix 5

Principles of research ethics review

A range of national and international guidelines on the conduct of ethical research studies have been published, including *The Nuremberg Code, the Declaration of Helsinki and The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research.*

Using international guidelines, Emanuel et al. proposed an ethical framework of seven principles, which provide coherent guidance to all clinical research stakeholders in all research settings. The principles are:

Value: The research study should have social, scientific or clinical value. The research study should be important, generalisable, and should include a plan for sharing results so that society can benefit. Resources should not be wasted on studies without integral value and human beings should not be exposed to risk without some scientific or social value.

Validity: The research study should be scientifically and methodologically sound and valid. The study, as designed and proposed, should be able to answer the research question. The Council for International Organisations of Medical Sciences guidelines explicitly state, "scientifically unsound research on human subjects is ipso facto unethical in that it may expose subjects to risks or inconvenience to no purpose." The research study should also be practically feasible and possible to execute.

Fair subject selection: The scientific goals of the study should determine who the participants or subjects are, as opposed to including a group of participants because they are either vulnerable or privileged. Likewise, exclusion of a group should not depend on convenience but on scientific objectives. Subjects should be selected in a manner that minimises risks and enhances benefits. Those who bear the risk of the **research study should enjoy its benefits and those who benefit should share the risk.**

Favourable risk–benefit ratio: Research is ethical if the potential risks to individual subjects are minimised, the potential benefits to individual subjects are enhanced, and the potential benefits to individual subjects and society are proportionate to or outweigh the risks. The requirement for a favourable risk–benefit ratio embodies the principles of non-maleficence and beneficence, long recognised as fundamental values of clinical research.

Independent review: Independent review by a committee not associated with

the research study helps to minimise the impact of potential conflicts of interest. Independent review also reassures the public and potential participants of the validity of the research.

Respect for persons: Individuals must be treated with respect from the time they are approached, throughout their participation, and when their participation ends. Respect involves having regard for the welfare, rights, beliefs, perceptions, and customs, both individual and collective, of individuals involved in research studies. Participants' information should be managed in accordance with confidentiality and privacy rules. Participants should be permitted to change their minds and withdraw from the study without penalty. They should be informed of any relevant new information that the study generates. Their welfare should be monitored throughout their participation. If subjects experience adverse reactions, they should be provided with appropriate treatment and removed from the study if necessary. Once the research study is over, it is best that there is a mechanism to inform participants of what was learned from the research.

Informed consent: Participants should be accurately informed of the purpose, methods, risks, benefits and alternatives to the research study. They must understand this information, and have the capacity to understand it and its bearing on their own clinical situation. They must make a voluntary and un-coerced autonomous decision to participate.