Standard Code of Practice for the HSE Research Governance, Management and Support Function – Roles and Responsibilities

Allocation and agreement on responsibilities by the relevant legal entity/entities by way of relevant legal agreements.

Allocating the roles and responsibilities of the different actors involved in a research study before the study starts is an important key step that will help to facilitate and clarify the overall governance requirements for a study and who is responsible for what.

When conducting a research study it is important to identify

- Who is responsible for what is done during the study (**Study Design**). In Clinical Trials a sponsor will be in place who will hold this responsibility.
- Who is/are responsible for how it is actually done (**Study Conduct**). For multi-site studies we need to identify
  - who is responsible for the overall study conduct at all the sites in the country (National Co-ordinating/Chief Investigator)
  - who is responsible for the conduct of a study at each site (Principal Investigators).
- Who is/ are the data controller/s and processors for the study (https://hseresearch.ie/data-protection-steps-to-follow/))

Note that terms such as Principal Investigator, Sponsor, etc are also used in the context of funding agencies for funded research projects. However where a Research study is part of a funded Research project the role and aligned responsibilities of the site Principal Investigator (PI), Chief/Co-Ordinating Investigator (CI) or Sponsor should not be confused with the role of project grant application or grant agreement Principal Investigator, Lead Investigator, Lead Institution etc. While the roles may be occupied by the same individuals/institutions it is not always the case.

Sponsor in Regulated and non-Regulated Clinical Trials

As per the HSE RGMS Framework, **all clinical trials[1] 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 term 'sponsor' is defined in the HSE RGMS Framework 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*"[2]. The Sponsor is responsible for study design.

[1] Clinical Trials as defined in the glossary of key terms and includes regulated and certain non-regulated studies.
[2] HRB's Clinical Trials and Interventions Research Governance Policy

It cannot be assumed that an organisation is a sponsor by default e.g. that the Principal Investigator's employer will automatically act as sponsor. Specifically for regulated clinical trials, the organisation must agree that they will assume and must have the capacity to fulfil the responsibilities of sponsorship via their sponsorship office.

Sponsorship in Regulated Clinical Trials

The sponsorship responsibilities for Regulated Clinical Trials i.e. CTIMPs and Clinical Investigations of medical/in vitro devices are governed by legislation and the 'sponsor' is further defined in regulated clinical trials as *any individual, company, institution or organisation which takes responsibility for the initiation, for the management and setting up of the financing of the regulated trial/investigation*.[3]

Sponsor's Legal representative in Regulated Clinical Trials

Where the sponsor of a regulated clinical trial or investigation is not established in the European Union, the sponsor shall ensure that a legal representative, established in the European Union is in place, as outlined in the relevant Regulations**Error! Bookmark not defined.**,[4]. Such legal representative shall be responsible for ensuring compliance with the sponsor's regulatory, obligations and will be the contact point for all communications with the sponsor outlined in the CTR, MDR and IVDR Regulations[3].

Co-Sponsors in Regulated Clinical Trials of Investigational Medicinal Products

The Regulated Clinical Trial Legislative Framework allows for a regulated clinical trial of an Investigational Medicinal Product[3] to have one or more sponsors (Co-Sponsors). Under the CTR all co-sponsors are jointly liable, with each co-sponsor taking complete regulatory responsibility for the whole clinical trial. However, co-sponsors may agree in a written contract which single sponsor will be responsible for the following tasks:

(i) compliance with a sponsor's obligations in the authorisation procedure;
(ii) a contact point for receiving and replying to questions from subjects, investigators or any Member State regarding the clinical trial;
(iii) implementing corrective measures imposed by any of the Member State Countries.

[3] 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
REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 on medical devices
REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 on in vitro diagnostic medical devices
[4] 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)

Co-sponsors may allocate among themselves, through a written contract, all remaining responsibilities but when a specific responsibility is not allocated, that responsibility remains with all co-sponsors and the principle of Joint responsibility applies.

Responsible legal entity for Insurance and Indemnity purposes

For studies that are not clinical trials5, formal sponsorship is not required. However it is fundamentally important to identify who is responsible for the study design and one party should take responsibility for this aspect of the study. This entity must take responsibility for ensuring that the appropriate indemnity for the Study is in place. (Reference to insurance and indemnity section)

The Principal Investigator

For avoidance of doubt the term Principal Investigator (PI) in this code refers to the person who has completed or is identified on the application to a Research Ethics Committee for a Research site. For multicentre studies there will be a PI responsible for each site and a National Co-ordinating/Chief Investigator (CI) with responsibility for the study at a country level. The National CI is usually also a site PI and this site is often referred to as the lead site (Figure 1). For international Studies, a Co-ordinating Investigator will also be in place with overall responsibility for the study. The individuals taking responsibility for these roles are usually named in the study protocol.

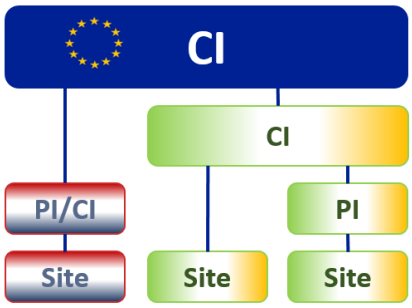

Figure1

In all studies the principal investigator (PI) is responsible for the day-to-day management and conduct of the research study at their research site[6]. The PI retains ultimate responsibility for the management of the research study, even if tasks are delegated to other research staff for example administrating a questionnaire or data entry may be completed by a member of the study team but the PI is responsible for ensuring that the study team member is suitably qualified/trained to complete these tasks and that the tasks are completed correctly and to the required standard. [7] For Regulated studies these responsibilities are outlined in regulations/legislation and Good Clinical Practice Guidelines such as ICH-GCP and ISO14155.

[5] Clinical Trials as defined in the glossary of key terms includes regulated and certain non-regulated trials.

[6] The Principal Investigator in signing this checklist for the study's application to the HSE Reference Research Ethics Committee: i) takes responsibility that all required data protection assessments, and recommendations from the research site(s) Data Protection Officer(s), has been completed accurately. ii) is responsible for checking that all investigators/researchers have ensured they have adequate insurance cover for the activities they will undertake as part of this research by contacting the relevant authority/insurance provider, iii) is responsible for both the standard and quality of this application and for the conduct of the research in accordance with the protocol and ethics committee application, iv)Is responsible for the conduct of the study in compliance with HSE policies and procedures

[7]CTR Investigator means an individual responsible for the conduct of a clinical trial at a clinical trial site;
Principal investigator means an investigator who is the responsible leader of a team of investigators who conduct a clinical trial at a clinical trial site

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For non-regulated studies in submitting an application to an ethics committee the PI is taking responsibility for the study for example the HSE Reference REC application checklist contains a PI's declaration.

If there is more than one Investigator at a site, they can be referred to as co-PIs, sub Investigators or Investigators. Co-PIs or members of the study team are delegated or designated responsibilities by the Site PI for the conduct of the Study at site but the overall responsibility remains with the Site PI.

	Overall (Investigator) responsible for the conduct of study*	Responsible (Investigator) for the conduct of the study at site	Designated or Delegated member of study team at site
Multi-site study	Co-ordinating Investigator	(Local/Site) Principal Investigator	Co- PIs, Co-Investigators, Sub-Investigators Study/Research Staff
Single Site study	Principal Investigator	Principal Investigator	Co- PIs, Co-Investigators, Sub-Investigators, Study/Research Staff
**Sponsor still has responsibility but some responsibilities lie with the PI/CI*			

Where research staff hold more than one affiliation, they must decide under which affiliation (i.e. the HSE or the academic/other organisation) they are acting when performing or undertaking their roles and responsibilities. This is particularly important for individuals with a dual appointment or employment contract. It is entirely possible for an individual to act in one role under an academic affiliation and a different role under their HSE affiliation once suitable underlying agreements governing data protection, material transfer, and IP considerations etc. are in place between the two institutions.

Research Site Responsible Officer

Refer to the HSE National Framework for Governance, Management and Support of Health Research [https://hseresearch.ie/wp-content/uploads/2021/09/HSE-Framework-for-the-Governance-Web-Optimised.pdf]

Division of Roles and Responsibilities

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As outlined in the HSE Framework, all parties collaborating on a clinical trial must, before starting the study, enter into an agreement that defines the roles and responsibilities of each of the organisations. While not a requirement, studies that are not clinical trials may also seek to put agreements in place that define the organisations involved roles and responsibilities.