Standard Code of Practice for the HSE Research Governance, Management and Support Function – Risk Assessment

Performing a risk assessment to permit proportionate oversight arrangements

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. The RGMS framework includes the following key principles:

- Institutional governance for individual research studies should be proportionate to the **level of risk**.
- Research activity needs to be registered and **risk assessed** before it commences.

Projects under the scope of the RGMS framework need to be assessed under three risk frameworks:

- Ethical risk assessment which permit low risk studies to be included in a proportionate review process. (see https://hseresearch.ie/wp-content/uploads/2022/02/Standard-Code-of-Governance-and-Management-Required-for-HSE-RRECs_-V0.9-PF.pdf)
- Data Protection Risk assessment by way of the Data Risk Scoring tool and when required the DPIA process
- Organisational risk assessment, which in due course will be carried out by the Regional research office but in the interim can be carried out by the host site via risk committees etc.

Ethical and Data protection risks are covered elsewhere, this document is looking at Organisational Risk before and during the research study life cycle.

The level and frequency of oversight for each research study during the life time of a project should be determined by and proportionate to the assessment of organisational risk prior to approval. To enable an assessment of organisational risk a Risk Assessment questionnaire and rating system has been developed and build as part of the RGMS standard application form (Appendix 4). This assessment is based on the NHS Research Risk Assessment Matrix Version 5 19.02.13 but drawing on a number of sources, that assigns a Risk Level; Low, Medium, High or Substantive to a study.

The Risk Assessment section of the form is designed to assess the potential organisational risk(s) associated with a specific study and provide a single Risk Level that reflects the study as a whole and which informs the next steps.

It is expected that the Risk Assessment section be completed by the Chief Investigator for multi-site study, the Principal Investigator for single site study or an appropriate delegate, in

communication with the research team members and if required with the relevant Research Office.

The risk assessment score will be reviewed by the relevant Research Office, together with the rest of the information provided via the RGMS Standard Application Form and accompanying uploaded documentation. This review will confirm or amend the risk score assessment by the applicant as Low, Medium High or Substantive Risk. Any factors, in place or proposed that eliminate, mitigate or transfer the risk should also be identified to inform the RGMS Function review process.

This review process should be supported by a Risk committee or equivalent group. A proportionate mechanism to manage the Risk should be put in place at local level. A suggested approach is outlined below. In this model the Regional Research office is described as the central point that coordinate this process. This can be done at local level in the interim until such offices are established.

Once the risk has been confirmed by the risk assessment process, different processes apply depending on the level of risk as indicated below.

Risk Level	Reviewed by	Approved by	Escalated to
Substantive	Director of Research RO Risk Committee Research Office	Regional Research Committee	Regional Senior Management Team
High	Director of Research Research Office	RO Risk Committee	Regional Research Committee
Medium	Research Office	Director of Research	RO Risk Committee
Low	Research Office	Research Office	Director of Research

Low Risk: The Regional Research office can expedite the assessment of low-risk research studies and recommend approval to a host site for sign-off by the appropriate authorised representative.

Medium Risk: Medium Risk studies should be reviewed by the Regional Director of Research or equivalent, who has the discretion to recommend approval by the host site, recommend

additional risk management strategies, or escalate for review by a relevant risk committee or equivalent. Following review of the risks inherent in the study and risk management in place and/or proposed, the Risk Committee can accept the risk and recommend to proceed or may recommend to proceed subject to additional risk mitigation measures. Such measures may include:

- Additional resourcing including financial
- Use of a Quality Management System,
- Mentoring of inexperienced PI
- A Formal Risk Management Plan put in place
- Recruitment/Assignment of an Experienced Research Manager
- Development of a Data Management Plan
- Additional Security Measures
- Involvement of a Trial Pharmacist
- Involvement of a Clinical Research Facility/Centre
- Involvement of a Clinical Research Organisation
- Study Monitoring Plan put in place
- Appointment of a Study Monitor
- Formal Site/Research Agreements in place
- Incorporation of specific requirements in relevant contracts.
- Additional Indemnity cover in place

High Risk: For decisions with regard to high-risk research studies the Regional Director of Research should be made by a relevant risk committee who can recommend to proceed as is, accepting the risk, or recommend to proceed subject to additional risk management or mitigation measures

In addition, the Regional Director of Research has the discretion to escalate a high risk study for review by the relevant Regional Research Governance Board or equivalent, presenting the risk elements of the study, any factors in place or proposed that eliminate, mitigate or transfer the risk and any risk management strategies recommended by the Risk Committee. Decisions can be made by the Regional Research Governance Board or equivalent to accept risk based on underlying factors such as the proposed mitigation measures, institutional risk appetite, strategic planning, organisation relationships etc.

Substantive Risk: All research studies with substantive risk should be escalated for review by the relevant Regional Research Governance Board or equivalent as per process outlined above.

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The RGMS function is responsible for ensuring that study governance and oversight, commensurate with the research study's risk and complexity, exists for the duration of the project life cycle up to when the research study can be deemed closed. Ongoing oversight may include monitoring (if appropriate), tracking and audit processes. Further details regarding the oversight of research studies during their life cycle will be developed in due course.

Initially the RGMS Function will facilitate a basic, check box compliance system, recording reporting requirements and requesting through an annual report if the required reports have been submitted. A fully developed oversight or compliance system should be proportionate to the risk level and regulatory status of the study. As the Research Office develops and is resourced research oversight will be put in place and may range from basic compliance checks for low risk studies i.e. submission of annual REC reporting to external auditing on behalf of the HSE. The principle of a Research Office oversight system is to assure and ensure commensurate levels of oversight are in place for research conducted within the Healthcare system. Duplication of any oversight arrangements already in place should be avoided where possible and the aim should be to identify and address any deficits between oversight required and oversight planned or in place.

Risk Questionnaire

Each of the 13 questions covers one potential area of risk or risk assessment and five options, numbered 1 to 5 are given to answer each question. To avoid confusion and to err on the side of caution if more than one option is applicable the applicants are directed to select the highest numbered option applicable.

- Option 1 is always the lowest level of potential risk and option 5 is the highest level of potential risk so that the unweighted score is from 1 to 5,
- A weighting is then applied to give the final weighted score for an individual question
- The Weightings are from 1 to 3 giving a possible overall range for any question of 1 to 5, 2 to 10 or 3 to 15.
- Once the weighting is applied the scores for each question can be added together to provide the total risk score for a study.

Study Protocol

Q. 1 Study Phase – Weighting 3

1. Not applicable i.e. not a regulated clinical trial or investigation
2. Phase IV, Post Approval Study
3. Phase III, Pivotal Study
4. Phase II

5. Phase I, Pilot Study

The lowest risk is assigned to studies that are non- regulated clinical trials or investigations. Risk is then assigned according to internationally recognised Clinical Trial Phase or Clinical Investigation Stage definitions.

Phase	Drug Study	Stage	Device Study
Phase I	Pharmacology 'First in human' Small Study (10's)to determine preliminary safety and dosage -	Pilot	Small study (10's) to determine preliminary safety and device performance
Phase II	Exploratory Large study (100's) to determine efficacy and adverse effects -		
Phase III	Confirmatory Larger study (1000's) to determine clinical efficacy and monitor adverse reactions	Pivotal	Large study (100's)to determine clinical efficacy and adverse effects
Phase IV	Post Marketing/ surveillance study to collect long term data on effectiveness and safety in general population	Post Approval	Post approval study to collect long-term data on effectiveness, safety and usage in general population

Q. 2 Scale of Research – Weighting 1

That is the total planned or estimated study recruitment across all Irish sites.

1. 0-20
2. 21-50
3. 51-100
4. 101-250
5. >250

This is designed to capture the scale of a research study, the rational is that the larger the number of participants the more resources required to conduct the study, provide oversight and the possible potential for error.

Q. 3 Study Population– Weighting 2

The Study population, as described in the protocol.

1. No research involvement of human study population e.g. secondary use of data, chart review etc.
2. Study population not considered vulnerable and who are healthy volunteers

3. Study population not considered vulnerable who are patients or service healthcare users
4. Study population considered vulnerable including women who are pregnant
5. High risk study population, i.e. receiving intensive care, significant health issues or concerns,

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This impacts on the potential risk of a study both for the governance required but also the actions needed to ensure the safety and wellbeing of the research participant who will mainly be Healthcare service users and/or patients of the HSE. Lowest risk is for studies who are not actively recruiting. Highest risk categorisation is given to vulnerable populations or those with the most complex healthcare needs.

A vulnerable population is a group of people that requires greater protection than normal against the potential risks of participating in research as they are more susceptible to social, psychological, legal, economic and physical harm. This will include such groups as children, drug users, runaways, prisoners, patients, victims of violence or the mentally ill.

The International Council of Harmonisation Good Clinical Practice Guidelines defines Vulnerable subjects/participants as Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

As an example the Research Ethics Committee standard form includes the following populations as vulnerable

- Children under 16 Adults with learning disabilities
- Adults who are unconscious
- Adults who have a terminal illness
- Adults in emergency situations
- Adults with mental illness
- Pregnant women / women of child bearing age
- Prisoners
- Adults suffering from dementia

- Those who could be considered to be vulnerable or have a particularly dependent relationship with the investigator, e.g. those in care homes, medical students.

While the study population may include individuals who are vulnerable without being classified as a vulnerable population, care should always be taken that if it is suspected/ or known that an individual approached, consented or participating in a study is vulnerable that their rights, safety and well-being are protected.

Q. 4. Research Intervention – Weighting 2

1. Non-intervention i.e. non-distressing data questionnaire
2. Intervention requiring Minor dose category of Ionising Radiation (IR), or low risk or non-invasive intervention i.e. low risk educational, food or cosmetic study, or intervention that is used in clinical practice or is standard care or potentially distressing data questionnaire
3. Intervention requiring Intermediate dose category of IR or invasive intervention that is used in clinical practice or is standard care i.e. medicine products used within their marketing authorisation
4. Intervention requiring Moderate dose category of IR or intervention is a significant change from standard care or involves withholding of elements of standard care
5. Intervention requiring Substantive dose category of IR or intervention has significant risk either a single high risk or highly invasive or distressing intervention or combination of interventions i.e. advanced therapy medicinal product

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Interventions can 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. Non Interventional research (data collection, observational) can include questionnaires, surveys, blood sampling or data collection (including monitoring) but does not attempt or intervene to effect outcome. The lowest risk is assigned to studies that do not contain an intervention i.e. observational or data collection studies. Risk is then assigned according to the potential for harm, mental and/or physical, of the research intervention(s). Cumulative harm is considered as are sensitive or distressing topics include those which might be considered personally intrusive such as illegal activities, sexual behaviours or experiences of abuse. Reference is made to the definitions contained in the HIQA Dose Constraints in Medical Exposures to Ionising Radiation 2020 https://www.hiqa.ie/reports-and-publications/guide/guidance-dose-constraints-medical-exposures-ionising-radiation. Standard of care is used as a bench mark which reflects that normal clinical practice can have inherent risks and that the research study may in of itself be of no more greater harm than the standard treatment or may be a comparison or study of standard treatments.

Q. 5 Study Specific Assessments or procedures – Weighting 2

1. No additional assessments
2. Survey or questionnaire based assessments, no clinical contact
3. Assessment requiring minor dose category of Ionising Radiation (IR) or is a non-invasive assessments for example blood pressure, temperature, height
4. Assessment requiring Intermediate dose category of IR or minor procedure(s) which is/are no more than minimally invasive e.g. taking additional blood samples, electrocardiogram (ECG)
5. Assessment requiring Moderate/Substantive dose category of IR or invasive or distressing procedure/assessment or series of procedures/assessments

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This question reflects that the assessments or procedures conducted during a study may of themselves have the potential for harm. An observational study may be non-interventional but may include blood sampling, an additional x-ray or a lumbar puncture each of which have a different risk profile.

Again reference is made to the definitions contained in the HIQA Dose Constraints in Medical Exposures to Ionising Radiation 2020. An invasive procedure is any procedure that pierces skin or mucous membrane or enters a body cavity or organ. This includes surgical entry into tissues, cavities or organs, or repair of traumatic injuries[1]. A minimally invasive medical procedure can be further defined as one that is carried out by entering the body through the skin or through a body cavity or anatomical opening, but with the smallest damage possible to these structures[2]. Non-invasive procedures are diagnostic techniques that do not involve the puncturing of the skin or incision, or the introduction into the body of foreign objects or materials.[3]

Study Conduct

Q. 6 Safety reporting – Weighting 1

1. Not required
2. Reporting as per REC guidelines only
3. Additional formalised system in place for safety reporting i.e. outlined in protocol/mandated by Sponsor
4. Regulated pharmacovigilance or medical device vigilance and reporting required
5. Regulated pharmacovigilance or medical device vigilance with high burden of reporting anticipated i.e. a high risk intervention or population

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This question is designed to categorise the burden of safety reporting required by the study and will contribute to the assessment of the organisational governance. The more intensive

[1] https://www.hse.ie/eng/services/publications/hospitals/hse-publications/code-of-practice-for-decontamination-of-reuable-invasive-medical-devices-7.pdf
[2] https://www.sciencedaily.com/terms/minimally_invasive_procedure.htm 2)
[3] Dorland's (2012). Dorland's Illustrated Medical Dictionary (32nd ed.). Elsevier. p. 955.

the safety reporting requirements, the higher the potential for error, and the more severe the consequences of that error and therefore the level of organisational governance required. The lowest level is assigned to studies that do not have a potential for safety issues and therefore a requirement for safety reporting and the higher levels are for regulated studies with legislative requirements for safety reporting and legal consequences for failures, errors or delays in reporting.

Q. 7 Follow-up - Weighting 1

1. No follow up required
2. Follow up in line with clinical or standard of care - no additional visits or contacts
3. Single visit or multiple remote follow up within 12 months
4. Extended multiple follow ups conducted remotely or at clinical visits over a number of years
5. Extended multiple follow-ups, some or all in person and not aligned to clinical care, over a number of years

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Follow-up is all post-treatment/active participation data that is collected per protocol i.e. to see if the short term effects of an intervention have continued after a certain period of time.). This can include study specific assessments, standard of Care (SOC) assessments or data collection/questionnaires. This question is designed to categorise the burden of follow-up required by the study and will contribute to the assessment of the organisational governance required and study burden or risk of conducting the study. The lowest level is assigned to studies that do not require a follow-up and the higher levels are for studies with extended, extensive follow ups.

Q. 8 Information / Personal Data - Weighting 2

1. Segregated and/or anonymised data only
2. Low (data) risk study or DPIA not required
3. DPIA completed. No concerns identified and no sharing of data required
4. DPIA completed, concerns identified i.e. joint/co data controllers, transfer outside EU or transfer of identifiable data
5. DPIA completed, data protection risk that cannot be mitigated

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This question is designed to be a high level assessment of possible data risk associated with the study and the governance requirements. Studies utilising only fully anonymised data are lowest risk and studies that require data sharing/transfer agreements and/or transfer outside the HSE environs of identifiable data or following Schrems II data transfers outside the EU are highest risk.

Q. 9 Consent - Weighting 1

1. Consent not required
2. Fully Informed documented Consent
3. HRCDC Consent Declaration required
4. Consent at vulnerable time or with time constraints
5. Consent from groups with limited capacity to consent or Proxy Consent with Assent

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This question is designed to be a high level assessment of possible risk associated with the consent process for the study and reflects the imperative that the **rights**, safety and being welling of the patient should be at the core of the Framework. Studies not requiring consent i.e. use of fully anonymised publically available data sets are lowest risk and studies that require consent from groups with limited capacity or a proxy consent are highest risk reflecting the additional cares that should be taken to protect the research participant.

Resourcing and supports

Q. 10 Investigator - Weighting 2

Note: Experience in this context refers to experience of conducting research studies of a type similar to the study proposed

1. Experienced PI who has completed at least two research projects of this level/scale
2. PI has research experience of this level/scale of research project
3. PI has research experience but not of this level/scale of research project
4. PI is not experienced but has participated in research projects of this level or scale i.e. as sub/co-investigator
5. PI is not experienced in the conduct of research of this level or scale

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The Principal Investigator has responsibility for the conduct of the study at site and for multicentre studies the Chief Investigator for the overall conduct of the study. Study risk is decreased as the experience and expertise of the CI/PI increases. Experience in this context refers to experience of conducting research studies of a type similar to the study proposed and is not related to clinical or academic expertise, experience or membership of professional bodies or publication history.

Q. 11 Research team - Weighting 1

Note: Experience in this context refers to experience of conducting research studies of a type similar to the study proposed.

Note: Support in this context refers to supports provided by external parties i.e. academic, commercial, other hospitals/sites.

1. Additional supports not required
2. Support needs of the study fully met - experienced dedicated research staff in place or agreed

3. Research team support required and budget available but not yet in place for example agreements required under discussion or additional training required
4. Research team support required but not fully budgeted or staff required not available/identifiable
5. Substantive research team support required but no budget available nor research team in place

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The Study risk increases if the study is not correctly and proportionally resourced be this financial, staff or support provided by the hospital healthcare facility service. This question references research team personnel provided by external parties i.e. academic, commercial, other hospitals/sites that support the conduct of the research study at site and their experience of conducting research studies of a type similar to the study proposed. While the issue of financial support for the study is dealt with elsewhere it is important to note that while funding may be available for research team support, there may be issues, perhaps transient, in identifying or making available the research team required

Q. 12 Hospital/Site/Service Support – Weighting 2

1. No supports required
2. Minimum additional support(s) required but available without a potential to impact on service delivery for example access to hospital/health service clinical space, additional routine blood sample processing/analysis by hospital clinical lab, additional blood sampling at time of clinical sampling, short survey, pre-screening of limited number of records
3. More than minimal additional support(s) required but available without a potential to impact on service delivery for example, multiple non-routine sampling/analysis, additional assessments or extensive questionnaires, access to archived healthcare records, pre-screening of large numbers of healthcare records.
4. More than minimal additional support(s) required with a potential to impact on service delivery i.e. an additional scan/x-ray, additional clinic visits, overnight stay.,
5. Substantive additional support(s) required with a potential to seriously impact on service delivery directly impacting patient/healthcare user care or waiting times, i.e. multiple additional scans/x-rays, multiple additional home/clinic visits, overnight stay.

This question is designed to capture the support, whether financially compensated or not required and provided by a site to a study. In this context additional support refers to access to staff, facilities, space, services, equipment, assessments or procedures required in addition to or outside of the clinical/healthcare service provided under standard of care by the hospital/site/service. If additional supports are required an agreement for or letter of support should be sought from each site/service. The higher the levels of support required and potential impact on the service delivery of a site the greater the risk of conducting the study both for the service as a whole but also the direct or indirect impact on healthcare users of the service.

Q. 13 Finance implications for the site – Weighting 2

1. No cost associated with the conduct of the study for the site(s)
2. Minimal cost implications, budget provided, discussed and agreed with site(s)
3. More than minimal cost implications, budget provided, discussed and agreed with
4. Cost implications not fully covered by budget or budget not discussed/agreed with
5. No budget provided and cost implications for site, additional staff, equipment, consumables, procedures outside clinical care

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Lastly the overall financial implications for the service are captured, this may be resourcing for additional support staff which may be provided and invoiced by an academic partner or additional, site provided, clinical procedures/assessment or facilities which would be outside the normal clinical treatment for a participant even if standard of care treatments for example electroencephalogram (EEG) are standard of care but may not be routinely offered in the study population. Lowest risk are studies without a cost for the site(s) associated with the conduct of the study and highest risk are studies with cost implications for site for example additional staff, equipment, consumables, procedures outside clinical care but without corresponding budgetary resources.

Overall Risk Score

Based on the weighting outlined for each question above the Overall Risk score is calculated by combining the individual weighted score for each question.

Over the 13 questions this will provide a minimum possible overall risk score of 20 and a maximum possible overall risk score of 100.

The overall score if it falls within the following ranges should be considered;

- Low Risk up to 40 % (Score 22 to 44)
- Medium risk 41 to 70 % (Score 45 to 77)
- High Risk 71 to 80 % (Score 78 to 88)
- Substantive Risk 81 to 100 % (Score 89 to 110)

	Criteria	Weighting	Option 1	Option 2	Option 3	Option 4	Option 5
	Protocol Questions						
1	*Study Phase*	**3**	**3**	**6**	**9**	**12**	**15**
2	*Scale of Research*	**1**	**1**	**2**	**3**	**4**	**5**
3	*Study Population*	**2**	**2**	**4**	**6**	**8**	**10**
4	*Research Intervention*	**2**	**2**	**4**	**6**	**8**	**10**

5	*Study Specific Assessments or procedures*	**2**	**2**	**4**	**6**	**8**	**10**
	Study Management questions						
6	*Safety reporting*	**1**	**1**	**2**	**3**	**4**	**5**
7	*Follow-up*	**1**	**1**	**2**	**3**	**4**	**5**
8	*Information / Personal Data*	**2**	**2**	**4**	**6**	**8**	**10**
9	*Consent*	**1**	**1**	**2**	**3**	**4**	**5**
	Resourcing and supports						
10	*Investigator*	**2**	**2**	**4**	**6**	**8**	**10**
11	*Research team*	**1**	**1**	**2**	**3**	**4**	**5**
12	*Hospital/Site/Service Support*	**2**	**2**	**4**	**6**	**8**	**10**
13	*Finance implications for the site*	**2**	**2**	**4**	**6**	**8**	**10**
	Minimum and Maximum		**22**				**110**