Definitive Interventions and Feasibility Awards (DIFA)

2020

Guidance Notes

Key Dates & Times	
Full applications open	06 April 2020
Full application closing date	13.00 on 7 July 2020
HRB Board decision	December 2020

25 May 2020 update: Following feedback from applicants in relation to the ongoing situation with Covid-19, the DIFA deadline will now remain open for applications until Tuesday 7th July at 13:00.
HRB will begin processing DIFA applications received from the original deadline of 30th June onwards, for those that wish to continue to work towards that timeline.

******The HRB expects applicants to contact their Host Institution as soon as they are invited to submit Full applications and engage with them to facilitate a review of the application, including any institutional risk assessment. This is in particular to enable review of the application for detailed costings, and any approval of a sponsorship role. Such processes may have changed since the last DIFA round, so please liaise with your Host Institution straight away to ensure you are fully aware of institutional requirements[1]. ******

[1] Many HRB Host Institutions contributed to the **Corporate Enabling of Clinical Research** initiative, which included work on common approaches to institutional risk assessments before taking on the role of clinical trial sponsor. For more information see the full 2019 report at **https://crdi.ie/corporate-enabling-of-clinical-research/**, and contact your Host Institution in relation to their specific requirements

*Applications must be completed and submitted through the HRB online Grant E-Management System (GEMs) (**https://grants.hrb.ie**), and this system will close automatically at the stated deadline and timeline listed above. Applicants are strongly recommended to read the 'Detailed guidance notes for applicants', appended to this document prior to completing the application form.*

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Definitive Interventions and Feasibility Awards 2020

Guidance Notes

1.0 Introduction

The Health Research Board (HRB) *Strategy 2016 – 2020: Research. Evidence. Action.*[2] launched in January 2016 highlights three areas of focus that the HRB will engage in during the course of this strategy. Focus Area 2 of the Strategic Plan aims to support the design, conduct and evaluation of healthcare intervention studies in order to improve health outcomes and health service delivery. Specific actions include funding healthcare intervention studies and providing support to strengthen the methodology and reporting of trials and intervention studies in Ireland.

2.0 Aims and objectives

The overarching **aim** of the DIFA scheme is to achieve tangible benefits to patients, peoples' health and health services through **support of studies evaluating a full scale, definitive trial of an intervention**. The evaluation may be of any appropriate design and will provide high quality evidence on the efficacy/effectiveness, cost and broad impact of the intervention. To achieve a pipeline of such studies, stand-alone **feasibility studies**[3] **conducted in preparation for a future definitive trial of an intervention** are also supported.

For the purpose of this scheme, we adopt the concept of **feasibility** as described by Eldridge *et al* (2016). Eldridge describes **'feasibility'** as an overarching concept, within which we distinguish between three distinct types of studies (1) randomised pilot studies (2) non-randomised pilot studies and (3) feasibility studies that are not pilot studies. This call is open to all types of stand-alone feasibility studies conducted in preparation for a future definitive trial of an intervention.

The **objectives** of the DIFA scheme are to:

- Fund research teams to conduct high quality definitive trials of interventions "definitive interventions", and feasibility studies in clinical and/or population health research and/or health services research that are relevant to health priorities internationally and/or nationally
- Support research that translates research knowledge into new ways of treating patients, delivering care or changing behaviour

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[2] *http://www.hrb.ie/publications/hrb-publication/publications//702/*

[3] *Sandra M. Eldridge et al. Defining Feasibility and Pilot studies in preparation for Randomised Controlled Trials: Development of a conceptual Framework. PLoS ONE 11(3): e0150205*

- Support conduct of trial methodology research within the context of proposed trials or feasibility studies
- Improve health outcomes and health service delivery

3.0 Scope

The DIFA scheme supports research that addresses questions of direct relevance to the improvement of patient care, health of the public and health services and that has strong potential to have immediate use for decision makers in everyday clinical practice or policy.

The term **intervention** includes any method used to promote health, prevent and treat disease and improve health care delivery. Examples include:

- Pharmaceuticals
- Procedures such as physiotherapy, surgical, radiation, speech and language therapy and others
- Medical devices
- Diagnostic tests
- Screening programmes
- Behavioural or psychological
- Educational
- Settings of care
- eHealth
- Other studies not listed above

HRB will support Regulated and non-regulated trials and other interventions, according to the published assessment criteria. No preference is given for any particular type of intervention.

We expect that evidence supporting the case for specific interventions has been gathered systematically, i.e. as systematic reviews or other evidence synthesis formats. Simple literature overviews are not sufficient. Evidence synthesised systematically to include evidence of (i) a systematic identification of previous work, (ii) critical appraisal, (iii) synthesis of the evidence and (iv) interpretation of findings'

The types of studies funded:

1. **"Definitive interventions"** of any appropriate design, including randomised controlled trials and non-randomized trials, designed to assess the efficacy/effectiveness, cost and broad impact of an intervention.
2. **Stand-alone feasibility studies** conducted in preparation for a future definitive intervention. The sole aim of funding these studies is to establish a pipeline for definitive interventions, therefore clear progression criteria to a substantive study are required. The applicant should indicate the proposed research question of the future substantive study. It is not possible to apply for a feasibility study, including a pilot study, and the associated definitive trial of the intervention at the same time.

Note: The scheme will also support **Studies within a trial (SWATs)** built into the main or feasibility study to explore primary trial methodology questions. To encourage and support further SWATs within the HRB-funded portfolio an additional amount of funding of up to €20,000, will be available towards identified costs of conducting a SWAT. At Full Application stage the applicant team may add or remove a SWAT.

Participation in **international studies** at feasibility stage and participation in full-scale international studies subject to evidence of feasibility within Irish sites is permitted. This may be the case where Ireland may be a recruitment site in an investigator-led trial, or alternatively where the team in Ireland is playing a leadership role in a potentially high-impact study. **Where the team in Ireland is not playing a key role in an individual trial, the applicants must clearly articulate the value for Ireland.** This may be, for example, gaining experience in delivering complex studies, establishing a collaboration for future studies, or enabling patient populations in Ireland to participate in trials which otherwise they could not access (e.g. in rare diseases).

Per patient costs outside of Ireland will not be eligible costs for the DIFA scheme. Exceptions may be made in the case of rare disease trials (where overall participant numbers may be low), or where per patient costs of participants from Low to Middle Income Countries are included. For international trials where Ireland is coordinating or sponsoring the trial, costs relating to sponsorship/trial coordination can be included (including insurance/indemnity, monitoring, shipping, statistical support, FAIR data management etc).

This scheme will not fund:

- Research involving animals
- Pre-clinical studies
- PhD Research
- Stand-alone systematic reviews
- Translational Research. Costs for sample collection and biobanking in the context of the intervention are allowed where justified, however costs for the analysis of samples are not
- Applications seeking to evaluate all phases of an intervention. Applicants must apply for feasibility studies separate to the associated full scale, definitive trial. Prior to considering funding for a definitive intervention trial, the review panel will request the results of feasibility work (with a discussion around acceptability, recruitment, compliance issues, delivery of the intervention, settings, recruitment and retention, effect size etc. as appropriate)
- Applications which are solely or predominately health service developments or implementation of an intervention without a predominant research element. The HRB will not fund the cost of providing the service or intervention itself, only the research element
- Applications from individuals applying for, holding, or employed under a research grant from the Tobacco industry
- Applications for research intended to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer

The HRB is a signatory of the All Trials campaign (**http://www.alltrials.net/**) and supports the aim of having all trials registered and all results reported. We extend this ambition to all interventions funded by the HRB. Unregistered and unreported interventions are unethical and cause harm because 1) the work may be repeated, 2) a metanalysis of published results will be skewed, potentially leading to flawed clinical decisions and 3) participants have a legitimate expectation that results will be published. We therefore require all HRB-

funded interventions to be registered in a publicly accessible register prior to initiation of the study. Results must be reported on the register within twelve months of completion of the intervention. The HRB also expects that results (positive and negative) of the intervention will be submitted for publication.

4.0 Funding available

The HRB plans to commit in the region of €18 million over the lifetime of the strategy (2016-2020) to support healthcare intervention studies. This is the third call of three rounds of funding. The number of awards made within each round will depend on the number of applications, the quality of applications submitted, and the amount requested per study type. Quality permitting, a **minimum of three definitive interventions** in addition to feasibility studies will be funded in this round.

The awards will support research proposals up to a maximum value of **€1,200,000** (inclusive of overheads) for Definitive Interventions, and typically **€380,000** (inclusive of overheads) or below for feasibility studies. Award durations of between 12-48 months (but not beyond 60 months) will be allowed. The HRB acknowledges that feasibility studies for complex interventions may incur higher costs than feasibility studies for RCTs. The cap of €380,000 for feasibility studies may be exceeded in exceptional cases where suitably justified.

An additional €20,000 (inclusive of overheads) can be requested for conducting a **SWAT**. This is in addition to the €1,200,000 overall budget.

The maximum value of an individual award for a definitive intervention has been increased from €1,000,000 in the previous round. This is to allow for additional costs arising from e.g. Research (FAIR) Data Management, Project Management/Trial coordination, Statistical expertise (as part of Applicant Team or costed appropriately), for the duration of the study as appropriate. Applicants should carefully review the HRB-CRCI budget checklist and get guidance on the budget at an early stage from their Host Institution or relevant Infrastructures to ensure the study is costed appropriately.

The budget requested and award duration of all proposals must reflect the scale and nature of the proposed research. Reviewers will thoroughly assess this when reviewing the proposal and will pay particular attention to feasibility studies in this respect. The maximum funding envelope available is **not** an invitation to apply for the maximum amount.

Note: The **proposed sponsor** must be named at Full application stage.

*Please refer to the HRB Clinical Trials and Interventions Research Governance Policy[4] for further details. Please note that **all trials and interventions** (Regulated and non-Regulated) directly funded by HRB will require a sponsor. HRB cannot act as the sponsor. The sponsor for HRB-funded trials cannot be an individual or company. Full details on the sponsor for the study, with a supporting document from the sponsoring institution will be required at submission of Full Application.*

[4] https://www.hrb.ie/funding/funding-schemes/before-you-apply/all-grant-policies/hrb-policy-on-clinical-trials-and-interventions-governance/

Where an application does not address the aims, objectives and scope of the call the application will be deemed ineligible and will not be accepted for review.

5.0 Applicant Team

5.1 Team Expertise

Applicants must demonstrate that the research team contains the necessary breadth and depth of expertise in all the methodological areas required to deliver the proposed study. Appropriate multi and inter disciplinary involvement in the research team is essential. As appropriate to the proposed study experts in trial methodology, statistics, trial management, health economics, PPI contributors, health service research, behavioural science, qualitative research methodologies, psychology, sociology etc. should be included as Co-Applicants or as official Collaborators. The Applicant Team has been made more flexible to allow for more Co-Applicants, in recognition of the growing size of the team necessary to deliver the study successfully). For studies that require substantial coordination, applicants should strongly consider the appointment of a study manager or coordinator (for small studies this may be one of your Co-Applicants rather than a dedicated post).

The HRB expects that applicants will collaborate, where appropriate, with partner organisations such as hospitals, health agencies, universities, local government, voluntary organisations and/or industry. The HRB encourages applicants to secure co-funding, where possible, from partner organisations. Applicants must also demonstrate the commitment of their partner organisations with evidence of existing partnerships and/or plans on how they will contribute to this award.

5.2 Lead/Co-Lead Applicant Eligibility

The **Lead Applicant** will serve as the primary point of contact for the HRB during the review process and on the award if successful. The Lead Applicant will be responsible for the scientific and technical direction of the research programme. She/he has primary fiduciary responsibility and accountability for carrying out the research within the funding limits awarded and in accordance with the terms and conditions of the HRB.

The Lead Applicant must:

- Hold a post (permanent or a contract that covers the duration of the award) in a HRB recognised Host Institution in the Republic of Ireland (the "Host Institution") as an independent investigator. For clinicians, an adjunct position in a HRB recognised Host Institution is acceptable **or**
- Be a contract researcher recognised by the Host institution as an independent investigator who will have a dedicated office and research space for the duration of award, for which he/she will be fully responsible, **or**
- Be an individual who will be recognised by the Host Institution upon receipt of a DIFA award as a contract researcher as defined above. The Lead Applicant does not necessarily need to be employed by the Host Institution at the time of the application submission.

They **must** show evidence of achievement as an independent researcher in their chosen research field by:

a) Demonstrating a record of research output, with at least three publications of original research in peer reviewed journals **and/or** evidence of expertise in conducting trials matched to the nature and context

of the project. Where appropriate, they should also provide evidence of other outputs such as published book chapters, reports to government and/or any other relevant outputs that have resulted in a significant impact in their field.

b) Demonstrating record of independence by showing that they have secured at least one peer-reviewed research grant for a research project/s, as either the Lead Applicant or a Co-Applicant. Funding received for travel to seminars/conferences and/or small personal bursaries will not be considered in this regard.

c) Show evidence that they possess the capability and authority to manage and supervise the research team.

Co-Lead Applicant option: where a **health and care practitioner investigator wishes to lead an application** and does not have the required academic track record to apply as Lead Applicant the applicant team may designate two **Co-Lead Applicants**, *at least one of whom must be a health and care practitioner practising in Ireland*. **One or both** will have to fulfil the typical requirements of a HRB Principal Investigator in terms of the expected academic track record (as set out in the eligibility requirements). Both are expected to demonstrate **relevant experience and expertise in clinical trials and other interventions.**

This option of Co-Lead Applicants is intended to allow health and care practitioner investigators, who may not have previously held research grants in their own name, to gain experience in leading such awards. This option may be particularly appropriate for feasibility studies, with a view to gaining experience for the future definitive trial. The Panel will be asked to review carefully the level of experience and expertise in the Applicant Team matched to the nature and complexity of the proposed trial or other intervention, and in particular being sensitive to the different objectives of a feasibility study compared with a definitive trial.

It is strongly recommended that the Lead Applicant(s) should have experience in the conduct of interventions. Only one application per Lead/Co-Lead Applicant to this scheme will be considered.

For applications utilizing the option of two Co-Lead Applicants, one Lead applicant must take on the role of submission to GEMs, their CV and contact details will be pulled through from GEMs. Co-Lead Applicants must enter their details manually. Co-Lead Applicants must review and approve the application prior to submission.

5.3 Co-Applicants & Collaborators

The DIFA 2020 round will allow for more flexibility between number of co-applicants and collaborators on the application, up to a maximum of 15 in total. The applicant team may be re-configured at Full Application (either to address a key gap identified by the Panel during their review, or to add a PPI co-applicant/collaborator), however the cap of a combination of 15 Co-applicants/collaborators will remain.

5.3.1 Co-Applicants

A Co-Applicant has a well-defined, critical and substantial role in the conduct and steering of the proposed research. Co-Applicants from outside of the Republic of Ireland are eligible, and welcome where such participation adds value to the proposed study. A Co-Applicant may receive funding for items such as running

costs and personnel. They will not receive support towards his/her own salary if they are in salaried positions. However, if they are not in a salaried position Co-Applicants can request their own salary or proportion of their salary, depending on their role and percentage of time dedicated to the research project. Each Co-Applicant must confirm their participation and is invited to view the application form online. We would not anticipate more than 10 **Co-Applicants** to be included (up to a **maximum of 15 co-applicants and collaborators in total**).

5.3.2 Collaborators

An official Collaborator is an individual or an organisation that provides an integral and discrete contribution (either direct or indirect) to the proposed research activities. A collaborator may provide material, training, access to specific equipment, specialist staff time, trials advice or other support, access to data and/or patients, instruments or protocols or may act in an advisory capacity. They can be based in an academic institution, a private enterprise, a healthcare organisation or agency, or come from the charity sector. Profile details must be provided for ALL official collaborators. In addition, each official collaborator must complete a **Collaboration Agreement Form** at full application stage. A template Collaborator Agreement form will be made available on GEMs for download. Collaborators may be based outside the Republic of Ireland. Up to **10 Research Collaborators** can be included (up to a **maximum of 15 co-applicants and collaborators in total**).

Relevant key gatekeepers should be named as Collaborators within your application form if the success of the study is dependent on access to

- Healthy volunteers or patients
- Vulnerable population groups
- Data or databases
- Existing national or international study (e.g. an existing cohort or longitudinal study or a clinical trial).

6.0 Other supports

6.1 Clinical research infrastructures

Applicants are expected to avail of the advice, trial and data management services and/or other forms of support from existing research infrastructures such as a Clinical Research Facility/Centre (CRF/CRC), Centre for Applied Medical Imaging (CAMI), HRB Clinical Research Co-ordination Ireland (HRB CRCI), the HRB Trials Methodology Research Network (HRB TMRN)[5] and/or a thematic HRB Clinical Trials Network (HRB CTN).

Applicants need to provide an **Infrastructure Agreement form** (including **national** and **international** infrastructures as required) at full application stage. The form sets out

- The nature and scope of the service or collaboration
- The rationale behind the choice of infrastructure and
- Any costs associated with the study (including those provided as in-kind contributions).

Please note: In line with the HRB Clinical Trials and Interventions Research Governance Policy **Regulated clinical trials** such as a clinical trial of an investigational medicinal product or a clinical investigation **must be**

[5] Support by the HRB-TMRN requires the inclusion of a primary methodological study within a trial (SWAT) or must include a non-standard novel trial design

conducted under the governance of a Clinical Research Facility/Clinical Research Centre (CRF/C), evidence of which must be provided to HRB in the form of a completed Infrastructure Agreement Form, setting out governance arrangements, signed bythe Director of the facility).

Applications which do not seek the advice and/or support from existing research infrastructure will be asked to justify why they have not done so.

6.2 Public and patient involvement (PPI) in research

Note: In line with the move to integrate PPI into HRB decision-making, HRB are currently planning a ***public review in DIFA 2020 of Full Applications.*** *This is planned to run in parallel with the international peer review. Comments from public reviewers will be provided to the applicants, and they will have the opportunity to respond to the public reviewer comments as part of the Right to Respond stage of review. While PPI is not a stand-alone scoring criterion in DIFA 2020, Panel reviewers will have sight of both the public review, alongside the scientific peer reviews, as well as the applicant team's response, thus it can inform the review of each application.*

HRB strongly promotes public and patient involvement (PPI) in the research that we fund. We use the definition of PPI proposed by INVOLVE UK (**www.invo.org.uk**): *Research carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them.* We also use the INVOLVE definition of the term 'public' which includes patients, potential patients, carers and people who use health and social care services as well as people from organisations that represent people who use services.

'Public and patient involvement' represents an active partnership between members of the public and patients as PPI contributors and researchers in the research process. This can include, for example, involvement in the choice of research topics, assisting in the design, advising on the research study or in carrying out the research. The HRB encourages a comprehensive approach to PPI. Those for whom benefit is intended should be at the heart of decision-making within the study.

PPI in research can improve quality and relevance. It can:

- provide a different perspective - even if you are an expert in your field, your knowledge and experience will be different to the experience of someone who is using a service or living with a health condition
- make the language and content of information such as questionnaires and information leaflets clear and accessible
- help to ensure that the methods proposed for the study are acceptable and sensitive to the situations of potential research participants
- help to ensure that the research uses outcomes that are important to the public and patients
- identify a wider set of research topics than if health or social care professionals had worked alone
- help you increase participation in your research by making it more acceptable to potential participants.

In addition to improving relevance and quality of research, it ensures that research is influenced by broader principles of citizenship, accountability and transparency.

PPI does not include the recruitment of study participants. This is participation of the public rather than involvement. It also does not include work aimed at raising awareness of the public around research, such as media publications of research findings, and outreach activities such as open days in research facilities.

In the application, you are asked to describe public or patient involvement in your research throughout the various stages of research design and planning, conduct, analysis and dissemination. We recognise that the nature and extent of active public or patient involvement is likely to vary depending on the context of each study or award. *For example, for the DIFA 2020 scheme, you may have actively involved patients in discussions on appropriate outcome measures, or on the proposed Core Outcome Set[6] for example.*

In this application, you must state whether **public or patient involvement** is included in the application and describe **(i) the purpose of the involvement, (ii) public or patient involvement to date and how that has influenced/changed what work has been planned, and (iii) public or patient involvement planned for the duration of the award.**

A number of useful resources for guiding researchers on public or patient involvement in research are provided in Appendix III including the Public Involvement Impact Assessment Framework (PiiAF), through which researchers can explore approaches to PPI and assess the impacts of involving members of the public in their research, and a Handbook developed by the European Patient Forum with practical examples for Lead Applicants of ways in which patients can be involved at different stages of a research project. Where members of the public or patient involvement are involved, they must be compensated for their time and contributions.

We strongly advise that you consult with your Host Institution who may be able to provide guidance and support on PPI in research.

6.3 Participation in international studies

For applications intended as part of an international study the applicants will be asked to provide details on the status, funding source, recruitment targets and outline the role of the Irish applicant as lead of the study or as participants. *Where the team in Ireland is not playing a leading role in an individual trial, the value for Ireland must be clearly articulated to the Panel; applications which do not do so will not be competitive.* Value for Ireland may be, for example, gaining experience in delivering complex studies, establishing a collaboration for future key studies, or enabling patient populations in Ireland to participate in trials which otherwise they could not access (e.g. in rare diseases).

Applicants as part of ongoing international trials will be required to provide a copy of the protocol at full application stage. This will greatly assist the reviewers and panel members in reviewing aspects of commitment and access and overall study feasibility.

Per patient costs outside of Ireland will not be eligible costs for DIFA 2020 scheme. Exceptions may be made in the case of rare disease trials (where overall participant numbers may be low), or where per patient costs of participants from Low to Middle Income Countries are included. For international trials where Ireland is

[6] An agreed standardized set of outcomes that should be measured and reported, as a minimum, in all clinical trials in a specific area of health. www.comet-initative.org

coordinating or sponsoring the trial, costs relating to sponsorship/trial coordination can be included (including insurance/indemnity, monitoring, shipping, statistical support, FAIR data management etc.).

7.0 FAIR Data Management

Data management/stewardship plans (DMP) are nowadays widely accepted as part of good research practice. The HRB is driving making of research data **FAIR** (**F**indable, **A**ccessible, **I**nteroperable and **R**e-usable) in order to benefit science by increasing the re-use of data and by promoting transparency and accountability. The **FAIR data principles**[7] provide a guideline for those wishing to enhance the re-usability of their data holdings: these principles put specific emphasis on enhancing the ability of machines to automatically find and use the data, in addition to supporting its re-use by individuals.

For researchers, the move to FAIR and open data means researchers need to consider data management issues and find suitable data repositories at the research planning stage. Applicants will have to provide some information about their plans for data management and data sharing at application stage. Please see Appendix V for supports at Host Institution level for this purpose.

The HRB's policy on management and sharing of research data[8] came into effect on 1st January 2020. In line with this policy, all **successful applicants will be required to submit a completed data management plan (DMP) to the HRB at the beginning of the study and a final updated version of the DMP with the final report at the end of the study.** The DMP will need to be submitted alongside a certification of approval from the designated representative(s) within the Host Institution. Successful applicants will be expected to use the HRB Data Management Plan template available through DMPOnline - **https://dmponline.dcc.ac.uk/**

The requirements of the HRB's DMP template can be found here:
https://dmponline.dcc.ac.uk/template_export/1814665590.pdf

8.0 Application and assessment process

Invited Full applications must be completed and submitted through the HRB online Grant E-Management System (GEMs) (https://grants.hrb.ie). GEMs will close the Full Application stage automatically at **1pm on 7 July 2020.**

The application must have been reviewed and approved by the signatory approver at the research office (or equivalent) in the host institution before it is submitted to the HRB. Therefore, applicants should ensure that they give the signatory approver sufficient time before the scheme closing date to review the application and approve it on GEMs. Please note that many host institutions specify internal deadlines for this procedure.

[7] https://www.force11.org/group/fairgroup/fairprinciples

[8] https://www.hrb.ie/funding/funding-schemes/before-you-apply/all-grant-policies/hrb-policy-on-management-and-sharing-of-research-data/

The HRB is committed to an open and transparent review process underpinned by quality, excellence and international peer review. To ensure the integrity of the assessment process, conflict of interest and confidentiality are applied rigorously at each stage of the process.

The **HRB Gender Policy** came into effect on 1 June 2016[9]. In line with international best practice the HRB has a responsibility to support both women and men to realise their full potential in order to ensure equality of opportunity and to maximise the quantity and the quality of research. To ensure fairness and equality to all applicants, each funding application received will be assessed as outlined in the call guidance documentation for that particular funding round.

A key objective of the HRB is to strive for gender balance in Irish health research. To ensure gender balance in decision-making, the HRB aims to reach the international best practice target of 40% of the under-represented sex in all HRB panels where possible. Gender will also be considered when appointing the position of Panel Chair. Gender balance of the Lead Applicant of the research team will be among the ranking factors to prioritise proposals with the same scores in the Panel ranking list.

Applicants to DIFA 2020 will be asked to carefully consider any potential **gender and/or sex differences** that may arise for the particular study, and how that will be accounted for during design, conduct, analysis and dissemination of the research.

8.1 Full application review process

A selected number of applicant teams will be invited to full application stage. Full applications must be submitted through the HRB online Grant E-Management System (GEMs) (https://grants.hrb.ie).

Information from the pre-application stage will feed automatically into the full application form. The Lead Applicant will have the opportunity to make revisions and to address the panel feedback from the pre-application stage as appropriate. Full applications should reflect a development of the relevant pre-application rather than a radically different approach. Revisions may include for example changes to the research team to address gaps in expertise, changes to work packages, changes to methodology, changes to budget.

Full applications will undergo a two-stage assessment process as follow:

8.1.1 Stage 1 – International Peer Reviewers

For each invited full application, the HRB aims to receive written feedback from at least three international peer reviewers. International peer reviewers play a vital role for the HRB in setting standards and in benchmarking our scientific community to enable them to operate in a global context.

[9] http://www.hrb.ie/research-strategy-funding/policies-guidelines-and-grant-conditions/policies-and-position-statements/gender-policy/

8.1.1 Stage 2 – Panel

The Full Application Panel will comprise of an independent Chair and six to ten members, selected from the DIFA Standing Panel. Members will have served on the Pre-Application Panel. Panel members are selected based on the range of applications received and the expertise and skillset required and have been appointed for this round (DIFA 2020), and the next planned round of the DIFA scheme.

Comments from public reviewers will be provided to the applicants, and they will have the opportunity to respond to the public reviewer comments as part of the Right to Respond stage of review. While **PPI** is not a stand-alone scoring criterion in DIFA 2020, this means that the Panel reviewers will have sight of both the public review, alongside scientific peer reviews, as well as the applicant team's response, thus it can inform the review of each application.

The reviewers will assess all full applications based on the following assessment criteria, which have equal weight. Successful applications must score highly in all criteria.

1. Case for the study
    - Important research question
    - Evidence supports the need for this study
2. Potential for impact of the study
    - Likely to impact on patients, public and/or healthcare system
3. Research team and environment
    - Appropriate skill mix and experience
    - Appropriate supports, infrastructures and research environment
4. Appropriate methodology
    - Study design and methodology will answer the research question
5. Feasibility of the study
    - Study will be delivered to time and on target
    - Resources are sufficient and reasonable

In addition, applicants should be aware that where there are serious ethical or safety concerns for participants in the study and these issues have not been addressed to the satisfaction of reviewers, such studies will not be supported.

The recommendations of the Full Application Panel will be presented for approval at the next scheduled HRB Board meeting. When the Board of the HRB has approved the process and recommendations, HRB staff will contact the applicants to notify them of the outcome.

9.0 GDPR

The **General Data Protection Regulation** (GDPR) came into force on 25 May 2018. As a result the applicant team will be asked through GEMs to **consent** that personal data provided as part of this application, including but not limited to CV information, may be shared with person(s) based outside of the European Economic Area

(EEA) for the specific purpose of obtaining peer reviews of this application. International reviewers play a vital role for the HRB in setting standards and in benchmarking our scientific community to enable them to operate in a global context. Individual peer reviewers are selected for their specific expertise in relation to submitted applications and can be based anywhere in the world.

Furthermore, by confirming participation, you will be asked to **consent** that HRB uses the information you provide (regarding all applicant team members) to consider your application, contact you about your application, and if you are successful, to manage your grant throughout its lifetime in accordance with HRB general T&C for research awards. This will include contacting you with regard to monitoring of progress through written reporting and other means e.g. interim review. We will publish some basic information on successful awards including PI, Host Institution, amount awarded and lay summary on our website and may highlight individual awards or researchers in more detail (with specific consent). We will also use the information you have provided to generate general statistics around our current funding portfolio, and to evaluate our funding mechanisms and investment. After your grant has ended, we will continue to keep your information on file (in accordance with HRB policies) to allow us to evaluate the outcomes, outputs and impacts of HRB investment in your research.

Please note that we will also use information associated with *unsuccessful* applications for a number of the purposes outlined above such as generating general statistics around our current funding portfolio, and to evaluate our funding mechanisms and investment e.g. demographics of applicants, research areas of applicants. Similarly, we will use the information provided about people employed on awards to help evaluate our career support and capacity-building initiatives.

10.0 The Health Research Regulations

Following the implementation of GDPR a regulation for health research known as the Health Research Regulations 2018[10] has been implemented in Ireland. These regulations outline the mandatory suitable and specific measures for the processing of personal data for the purposes of health research and reinforce the fact that **explicit consent** should always be the legal basis for health research when using identifiable, sensitive data unless a consent declaration is obtained from the newly appointed Consent Declaration Committee[11].

11.0 Timeframe

Full Application Stage	
Mid/Late April	DIFA applicant workshop (pre-recorded webinar)
7th July 2020	Deadline for submission of full applications[12]

[10] http://www.irishstatutebook.ie/eli/2018/si/314/made/en/pdf
[11] https://hrcdc.ie/
[12] The deadline for Full Applications will be kept under review, depending how the situation with Covid-19 evolves in Ireland

September 2020	End of peer-review
September/October 2020	Right to reply phase (14 calendar days)
November 2020	Full proposal panel meeting
December 2020	Board approval
May 2021	Earliest start date of awards

12.0 Contact

For further information on the **Definitive Interventions and Feasibility Awards** contact:

Dr Susan Quinn
Project Officer
Health Research Board
e **squinn@hrb.ie**
t +353 1 2345 139

Dr Caitriona Creely
Programme Manager
Health Research Board

The HRB reserves the right to reject any application that does not meet the terms of this call. The HRB's procedure for appealing funding decisions is available at http://www.hrb.ie/research-strategy-funding/policies-guidelines-and-grant-conditions/policies-and-position-statements/

Appendix I: Updated Detailed Guidance on the Full Application Form

Please review carefully as changes have been made from the guidance provided at pre-application stage

Information from the pre-application stage will feed automatically into the DIFA Full Application form and can be edited as required. In many cases the word count for Full Application will have increased significantly, so information provided in these sections should be expanded accordingly.

Only registered users of the GEMs system can apply for grants. In order to submit an online application to the HRB, applicants are required to register at the following address: **https://grants.hrb.ie**
Please refer to the GEMs Technical Guidance Note for further information.

The Lead Applicant must create the application, but it can then be jointly completed with named Co-Lead (if applicable) and Co-Applicants. **For applications utilising the option of two Co-Lead Applicants (only available where one co-lead is a health and care practitioner), one Lead applicant must take on the role of submission to GEMs. Both Co-Lead Applicants must review and approve the application prior to submission.**

- Lead Applicants can register on GEMs and they will receive an email to confirm their registration and log in details. The Lead Applicant can then add information on their contact and CV details in 'Manage My Details' section of GEMs.
- Lead Applicants previously registered on GEMs can login to GEMs and update any information regarding their contact and CV details in 'Manage my details'.

Once logged in to GEMs applicants are taken directly to the Home page which is the starting point to create a new Grant application. Please select the Definitive Interventions and Feasibility Awards (DIFA). ***Further details for completing each of the main sections of application form is provided below:***

Declaration of Interests

Please declare any conflict of interests or potential conflict of interest that a member of the applicant team may have, e.g. a personal or commercial interest in the study. Please give details where a member of the applicant team (including but not exclusively any industry partners) has previously been involved in the design and/or development of the product/service/application being evaluated (e.g. an App to deliver an education programme).

Host Institution and Signatory Notification

The HRB expects applicants to contact their Host Institution as soon as they are invited to submit Full applications and engage with them to facilitate a review of the application, including any institutional risk assessment. This is in particular to enable review of the application for detailed costings, and any approval of a sponsorship role. Such processes may have changed since the last DIFA round, so please liaise with your Host Institution straight away to ensure you are fully aware of institutional requirements.

Host Institution

Your Host Institution (HI) will be automatically included as per your pre-application form. The Host Institution (HI) for the HRB award is a HRB recognised host institution in the Republic of Ireland. This is normally that of the Lead Applicant, but it may be another organisation/institution designated by the research team, where it is clearly justified.

An up to date list can be found at all times at **http://www.hrb.ie/research-strategy-funding/policies-guidelines-and-grant-conditions/policies-and-position-statements/approval-of-host-institutions/**

Signatory Notification (within Host Institution)

The HI signatory is automatically included as per your pre-application form. Once the Host Institution is selected at pre- application stage this will link the authorised signatory (Dean of Research or equivalent person authorised to endorse research grant applications for the Host Institution) in that Host Institution to the Lead Applicant's application form. An automatic email is not generated at this point and the HRB strongly recommend that the applicant notify their HI of their intention to submit an application to the DIFA 2020. **We recommend that you notify the HI signatory of your intention to apply as soon as possible in the application process.** The HI signatory has confirmed at pre-application stage their willingness to participate as HI for the application through GEMs and a PDF of the application will be available for them to review with a view to them ultimately approving the final version for submission to the HRB.

1.0 Lead Applicant, Co-Lead Applicant, Co-Applicants and Collaborators details

1.0 Are you using the Co-Lead Applicant option? (Y/N)

Please note, this option is only available where at least one of the Co-Leads is a Health and Care Practitioner researcher practising in Ireland.

For applications utilising the option of two Co-Lead Applicants, the same information will be requested for each person. One Lead applicant must take on the role of submission to GEMs, their CV and contact details will be pulled through from GEMs. Co-Lead Applicants must enter their details manually. **Co-Lead Applicants must review and approve the application prior to submission.**

1.1 Lead Applicant

Details are requested about the Lead Applicant, including their position, employment status (contract or permanent), whether they are seeking salary-related costs, and their experience.

Please note that a letter of support from the Host Institution must be provided if a Lead Applicant is in a contract position. This letter should originate from the Head of Department (or equivalent signatory), on headed paper, confirm current employment status and duration of contract, provide assurance of candidates experience and eligibility for this award and the Host Institutions willingness to host the candidates research should they be successful in this funding call.

The Lead Applicant's **contact and CV details** (Name, contact information, institution, present position, employment history, profession and membership of professional bodies) are managed in the 'manage my details' section of GEMs and are automatically included in any application created involving that individual.

Publications and Funding Record

You are asked to add your **10 most relevant publications to this application** on which you have acted as senior author. Please use the publication selection tool in this section to select the 10 most relevant publications. You should also include your **5 most relevant funding** awards as Lead Applicant or co-applicant. Please note your funding record will **not** be pulled through from your CV to the application form.

Additional evidence of experience and expertise relevant to this application

The Lead Applicant(s) may also wish to include any additional experience or expertise that will support their application. For example, elaborate on their previous experience of conducting or evaluating trials and interventions. The word limit is **300 words**.

1.2 Co-Lead Applicant (if applicable)

Please note, this option is only available where at least one of the Co-Leads is a Health and Care Practitioner researcher practicing in Ireland. Details are requested about the Co-Lead Applicant and must be entered manually, including their name, contact information, institution, present position, employment history, profession and membership of professional bodies position, employment status (contract or permanent), whether they are seeking salary-related costs, and their experience.

1.3 Co-Applicants

The Lead Applicant can add up to 10 Co-Applicants to an application by entering their name on GEMs, (up to a maximum of 15 co-applicants and collaborators in total.
Co-applicants added at Pre-Application stage are carried over to the Full Application form. Co-Applicants must approve the DIFA Full Application before submission but will not automatically receive an email to inform them of this. **It is the responsibility of the Lead Applicant to contact their Co-Applicants to request that they log in and decide whether to accept or reject their participation and consent to the Full Application being submitted jointly in their name.**

The Lead Applicant may change a Co-Applicant from Pre to Full Application stage and this must be suitably justified in the section 'Details of the Research team'. To add a new co-applicant, enter their name on GEMs. If the Co-Applicant is already registered on GEMs, the system will find them and will allow the Lead Applicant to select them. Alternatively, a co-applicant can be added manually by entering their name and email details. GEMs will send them an email with login details for completing the registration process and in the case of a new Co-Applicant will inform them that they have been invited by the Lead Applicant to participate on the application as a co-applicant. PPI Participants can register in the same way as Co-Applicants.

Registered co-applicants can then manage/update their contact details and CVs in 'Manage My Details' and they can decide whether to accept or reject their participation and consent to the application being submitted jointly in their name. If a co-applicant rejects participation on an application the Lead Applicant is informed and may revise the application accordingly. Co-applicants which accept to participate in an application can

edit the application. The system will flag through a pop-up warning if another user is working on the application form at the same time. A member of the applicant team may choose to over-ride this pop-up message and continue to enter data but it advisable that they contact the other person directly to avoid losing data when applying the override function.

Host Institution Letters of Support must be provided for **(1) all Lead Applicants in a contract position and (2) Co-Applicants in a contract position who are seeking their own salary.** The formal letter on headed notepaper, dated and signed by the Head of School/Research Centre/Hospital must include the following information; [*Host Institution – insert name*] which is the host institution of [*applicant - insert name*] confirms that [*applicant - insert name*]: (i) holds an employment contract which extends until [*insert date*] or will be recognized by the host institution upon receipt of the HRB ILP award as a contract researcher; (ii) has an independent office and research space/facilities for which he/she is fully responsible for at least the duration of the award, and (iii) has the capability and authority to mentor and supervise post-graduate students and post-doctorate researchers. Electronic signatures are acceptable for letters that are uploaded on the HRB GEMs system.

It is the responsibility of the Lead Applicant to ensure that applications are completed in full and all necessary documentation is received by the HRB on, or before, the closing dates indicated.

1.3.1 Co-Applicants Contact and CV Details

Each co-applicant can manage their **contact and CV details** (Name, contact information, institution, present position, employment history, profession and membership details of professional bodies) under 'Manage my Details' section of GEMs and this information will be automatically included in any application that involves this individual. **Publications and Funding Record** (5 most relevant publications in peer-reviewed journals and details of 5 past or current grants held (including HRB grants) where the applicant has acted as Lead Applicant or co-applicant) which are most relevant to this application must be added by the Lead applicant under 'add further co-applicant details', and will **not** be pulled through from co-applicant CVs. Please state the total number of the co-applicant's peer reviewed publications.

1.4 Collaborators Details

The collaborators added at pre-application stage can be viewed in Section 4.5 'Details of the Research Team'. The Lead Applicant may change a Collaborator from Pre to Full Application stage and this must be suitably justified in the section 'Details of the Research team'. The Lead Applicant can add up to 10 collaborators per application (up to a maximum of 15 co-applicants and collaborators in total). Unlike co-applicants, the information for collaborators is not automatically drawn from the 'Manage my Details' section of GEMs but must be entered by the Lead Applicant. The Lead Applicant must enter **contact and CV details** for all collaborators including name, contact information, institution, present position, employment history, profession and membership details of professional bodies, **Publications and Funding Record** (if applicable) (five most relevant publications in peer-reviewed journals and details of 5 past or current grants held (including HRB grants) relevant to this application where the collaborator has acted as Lead Applicant or Co-Applicant).

In addition**,** for each collaborator a signed **Collaboration Agreement Form** must be provided. A template Collaboration Agreement Form is available for downloaded from GEMs. Forms must be completed, signed,

dated and uploaded where indicated on HRB GEMs. Electronic signatures are acceptable on letters/forms that are uploaded on GEMs.

2.0 Study Details

2.1 Study Title

This should be descriptive, concise and should reflect the aim of the study by identifying the study design, the subject population and interventions to be examined.

2.2 Research Question

Clearly state the research question behind the proposed work. Where the research question for the future DI will be different (in the case of feasibility studies), please also set this out. The word limit is **100 words**.

Briefly explain the study phrased in PICO[13] terms, with reference to the **main research question** (as applicable to your study type):

Population: target population
Intervention: represents the Intervention of interest
Control or comparison: Usually the standard intervention or no intervention
Outcome: expected outcome, leading to effectiveness and cost-effectiveness

The word limit is **100 words.**

Have you searched the COMET database to check whether a Core Outcome Set[14] has been agreed for this area of health? Y/N

Have patients/patient organisations been involved in the development of outcome measures for this study[15] (as appropriate) Y/N

2.3 Acronym

Acronym is optional.

2.4 Study Duration and Start date

Please indicate the expected length of the proposed study in months and the proposed start date. The HRB expects these awards will typically be between 24 to 48 months in duration (but can be between 12 and 60 months). The earliest start date is May 2021.

2.5 Study Lay Summary

This lay summary is similar to the project abstract in that you are asked to describe what you propose to do; say why you think it is important to complete this piece of work and how you are going to go about conducting, analysing and drawing conclusions from the research. It should be written as a plain English summary such that it is clear, easy to understand, and is easily accessible to a lay audience. It should not be copied and pasted

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[13] *Nobre MR, Bernardo WM, Jatene FB. Evidence based clinical practice. Part 1—well-structured clinical questions. Rev Assoc Med Bras 2003 October-December; 49(4):445-9.*

[14] An agreed standardized set of outcomes that should be measured and reported, as a minimum, in all clinical trials in a specific area of health. www.comet-initative.org

[15] Plain language animation on outcome sets produced by COMET **http://www.comet-initiative.org/resources/PlainLanguageSummary**

from elsewhere in the application. The lay summary may be used when providing information to the public with regards to the variety of research funded by the HRB and may be posted on the HRB website. It will be reviewed as part of the public review described in the application and assessment process. A well-written lay summary will enable peer reviewers and Panel members to have a better understanding of your research proposal. The word limit is **300 words**.

2.6 Study Abstract

This should be a succinct summary of the proposed research. The aims and hypotheses of the study should be conveyed with clarity. The objectives of the study and what the work is expected to establish should be described. Ideally it provides a clear synopsis of your proposal and should set the research proposal in context. Please label the project as a definitive intervention or as a feasibility study. The word limit is **350 words**.

2.7 Study Type

2.7.1 The study type selected at pre-application stage will feed through into the full application form. It is expected that this will remain the same, with exception of cases where applications intend to add or remove a SWAT.

2.7.2 Is this a regulated or non-regulated study?
Regulated clinical trials much be conducted under the governance of a CRF/C.
Please upload the Infrastructure Agreement form signed by the CRF/C Director detailing these arrangements in Section 5: Infrastructure and Support

3.0 Study Description

Please note that the information submitted at Pre-Application stage under the question 'Project Description' will be in a section at the top of this page. This information will **not be visible** to the reviewers/Panel and is for your information purposes only. For the Full Application the Lead Applicant must populate each of the sections within the Project Description.
Please ensure that your application is focused and that sufficient evidence is provided to enable the international peer reviewers and grant selection panel members to reach a considered judgement as to the quality of your research proposal, its scientific quality, research team expertise, relevance and potential impact of the study.

The Study Description should include:

- Relevance and rationale for research based on systematically gathered evidence from the literature
- Evidence from previous feasibility studies (for DIs)
- International Study information
- Overall aim
- Objectives and deliverables (including Gantt chart, see template provided)
- Changes from Pre-Application
- Research design and methodological approach, including participant flow diagram
- Discontinuation criteria
- Internal pilots (if applicable)
- SWAT
- Public and Patient Involvement

- Impact statement
- FAIR Data Management and Stewardship
- IP considerations
- Trial management, Governance and Safety Monitoring
- Participants involved in trial delivery, and trial experience
- Potential risks and ethical concerns
- Biobanking issues
- Sex and/or Gender issues in the study
- Dissemination and knowledge exchange Plan

3.1 Relevance and Rationale for Proposed Research

Describe the background to the research proposal and detail the size and nature of the issue to be addressed. Please address the following:

- State the principal research question being asked.
- What is the rationale for the study?
- Why is this intervention needed? What problem is being addressed? Justify the necessity for the research, both in terms of timeliness and relevance to health of patients/public/health system especially in an Irish context.
- Please address potential benefits and potential harm of the proposed intervention.
- Will the results be generalizable beyond the research setting of the study?

The word limit is **1500 words.**

3.2 Are any relevant studies listed on international registries?

(e.g. European Clinical Trials Database (EudraCT), International Clinical Trials Registry Platform (ICTRP). If yes, please provide study registration number(s).

3.3 Describe the systematically gathered evidence base for this research such as relevant systematic reviews and other formats of evidence synthesis.

Evidence synthesised systematically to include evidence of (i) a systematic identification of previous work, (ii) critical appraisal, (iii) synthesis of the evidence and (iv) interpretation of findings. Demonstrate why your research is important now, both in terms of time and relevance. Where no relevant published systematic review exists, it is expected that the applicants will undertake a satisfactory review of the currently available evidence using systematic techniques. Simple literature overviews are not sufficient. Applicants must provide a protocol to show how the search was conducted, including literature and clinical trials registries.

The proposed standard for what constitutes a satisfactory review of the existing evidence to inform your research proposal is as follows:

- A relevant Cochrane Systematic Review **or**
- If no Cochrane Review exists, then another systematic review that is published in a peer reviewed journal **or**
- If no published systematic review is identified, then the Lead Applicant and research team should present the findings of a systematic review that they have undertaken for the purposes of the application. Importantly, in this case applicants are required to provide sufficient details of the

methodologies employed to allow evaluate confidence in the findings and to allow the review to be replicated. Simple literature overviews are not sufficient.

- Additional evidence may be provided through formal input from relevant Irish patients, service users or carers. However, this does not substitute for systematically gathered evidence.

The word limit is **750 words.**

3.4 Evidence from previous feasibility studies (compulsory for DI Study)

Include relevant information from previously conducted feasibility studies.
Please address all the following:

- Describe clearly but succinctly the work that was carried out, when, on what groups in which settings and what was learned that facilitated the development of the protocol for the final definitive study.
- Provide details on the screening and recruitment rates achieved during the feasibility study.
- Were progression criteria met?
- Provide assurances that you are confident that the intervention can be consistently implemented as intended.

The word limit is **500 words.**

3.5 Pathway to a future DI (compulsory for Feasibility Study)

Provide a brief description of a possible definitive trial of an intervention based on outputs from this proposed feasibility study. Propose **clear progression criteria** towards the definitive trial.
The word limit is **500 words.**

3.6 International study

If your research proposal is part of a larger international study, please upload the full protocol and provide a summary of progress to date. If the study is live, please provide a letter from the chair of the Independent Data Monitoring Committee (IDMC) outlining how the recruitment is progressing and any issues that may be relevant for reviewers.

If your proposal is to add Irish sites to an international study, please make a clear case for undertaking this study in an Irish setting. State with clarity the projected recruitment numbers for the trial overall, and the projected recruitment numbers from Ireland (at the sites listed in sections 3.19). Clarify the funding status of the main study, whether it is powered adequately without the Irish component, and clearly articulate how participation from Ireland will add value to the study (e.g. by increasing generalisability to different healthcare settings, including a different sub-population etc.).

Clearly outline what the role of the participants from Ireland will be in the context of the International study (aside from recruitment), and what role the international lead/partner will take in relation to the study in Ireland. The role of the IDMC is outlined in Appendix IV.
The word limit is **500 words.**

3.7 Overall Aim

Please state the overall aim of the research, with reference to the main research question stated in Q2.2.
The word limit is **150 words.**

3.8 Objectives and deliverables

Please add a minimum of three research objectives. Objectives should be SMART (specific, measurable, achievable, realistic and time-bound) and appropriate for the definitive or feasibility nature of the proposed study. For each objective, list a subset of deliverables which will be used to monitor progress throughout the lifetime of the award if successful. Objectives/deliverables should be mapped against estimated completion timelines in a Gantt chart, and any milestones highlighted.

NB: Two Deliverables (minimum) for a Data Management Plan must be included: one at study start, one at the end of the study.
The word limit is **60 words for each objective and 150 words for the deliverables**.

You **must upload a Gantt chart** that lists the above objectives and deliverables against the estimated timelines for completion, together with any additional milestones/key dates (Figure 1). Please ensure that care is taken to account for the study start-up time, patient screening and/or recruitment time in the Gantt chart.

Sample Gantt (edit as appropriate)	Project Year 1				Project Year 2				Project Year 3				Project Year 4			
Calendar Timeline																
Work Package 1: (Title)	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
1.1: e.g. ethics submission/approval		◆	◆													
1.2: e.g. staff recruitment/training	◆	◆	◆													
1.3: e.g. data collection		◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆
1.4: e.g. data analysis					◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆	◆
1.5: e.g. dissemination														◆	◆	◆
Work Package 2: (Title)	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
2.1:																
2.2:																
2.3:																
2.4:																
2.5:																
Work Package 3: (Title)	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
3.1:																
3.2:																
3.3:																
3.4:																
3.5:																
Work Package 4: (Title)	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
4.1:																
4.2:																
4.3:																
4.4:																
4.5:																

Legend
Time that work is expected to take place on a work-package/objective = ◆
Calendar Timeline: Shade boxes black up to current calendar date on project.
Work-package/objective progress: Shade boxes green up to current stage to indicate progress on objective to date. As in example above, this can indicate where project is ahead of schedule.

Figure 1: Example of Gantt chart template available from the HRB.

3.9 Changes from Pre-application

Please clearly describe any changes from the pre-application submitted. In particular address the **Panel feedback**, specifying how feedback has been considered for the Full Application. Reference any new developments relevant to your proposed study that have arisen since the Pre-application was submitted, including other trials that have reported, or emerging evidence which would have a bearing on your proposal. Please clearly justify where changes have impacted on the proposed costs and/or duration of the research.
The word limit is **600 words.**

3.10 Research Design and Methodological Approach

The information added at Pre-Application stage under 'brief overview of research design and methodological approach' will be visible here and should be expanded on significantly to give detailed information on the research design and methodology as per the question below.

Summarise the proposed research plan, providing descriptions of any individual work packages and describe how they integrate to form a coherent research project. Include details of the general experimental approaches, study designs and techniques that will be used. Include details on all stages of the study design including rationale for sampling strategy, justification of sample size and power calculation, details on the design chosen and the intervention, the methods of data collection, measures, instruments and techniques of analysis for quantitative and qualitative designs, outcomes measures, cost effectiveness and data analysis/management plans as appropriate.

Please clearly describe the **healthcare setting** and **how participants will be accessed** as all reviewers will be from outside the Irish healthcare system.

Justify the **choice** of your planned intervention. Please consider following the TIDieR[16] checklist and guide for describing the intervention.

Describe and justify the **design** chosen, the methods you plan to use and the rationale of your choice. Show how your research design will allow you to answer your research question. You are expected to seek advice and input from an experienced research design and statistics expert at study design phase.

Please address the following and consider reviewing Appendix II:

- If this is a feasibility study, state explicitly the type of feasibility (see *Eldridge et al 2016*)
- What is the proposed study design (e.g. randomised or non-randomised, conventional parallel group RCT as opposed to cluster, factorial or stepped-wedge design etc.)?
- Describe the population to be studied
- Please consider the age and gender of participants and clearly justify exclusions
- Is subgroup-analysis by gender planned?
- Briefly explain sex and/or gender issues in this study. (See further question 3.24)
- Do the proposed subjects represent your target population?
- What is the planned intervention?
- Have you fully described 'usual care' (if appropriate)?
- Describe the healthcare setting in which the intervention will be delivered
- What are the proposed practical arrangements for allocating participants to study groups?
- What are the proposed methods for protecting against sources of bias?
- How variable is the intervention – between sites, over time etc.?
- Are there aspects of context and/or the environment which may impact on the evaluation being undertaken?
- What are the planned inclusion/exclusion criteria?

[16] *Hoffmann T et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ. 2014;348:g1687*

- What is the proposed duration of intervention period?
- What is the proposed frequency and duration of follow up?
- Discuss the reliability and validity of all study instruments and scales for the intended population
- What are the proposed primary and secondary outcome measures? For surrogate outcome measures, provide evidence of validity. Was patient/patient representatives input sought in relation to the outcome measures?
- Show how the outcome measures chosen will ensure clinical relevance as well as relevance for the patient/target population.
- How will the outcome measures be measured at follow up?
- Are you planning to include health economics and quality of life measures? If yes, provide full details regarding the type of analysis to be undertaken, the rationale of the design proposed, the personnel who will conduct analysis, power calculations and inclusion/exclusion criteria. In cases where one or both of these measures will not be addressed in this study, please explain why.
- What size of the difference is the trial powered to detect?[17]
- What is the proposed sample size and what is the justification for the assumptions underlying the power calculations? Include for both control and intervention groups, a brief description of the power calculations detailing the outcome measures on which these have been based, and give event rates, means and medians etc. as appropriate
- What is the planned recruitment rate? How will the recruitment be organised? Over what time period will recruitment take place?
- What evidence is there that the planned recruitment rate is achievable?
- Are there likely to be any problems with compliance? On what evidence are the compliance figures based?
- What is the likely rate of loss to follow up? On what evidence is the loss to follow-up rate based?
- How many centres will be involved (specify national and international as appropriate)?
- Has acceptability testing been considered?
- What is the proposed type of analyses?
- What is the proposed frequency of analyses?
- Are there any planned subgroup analyses?
- Do you plan a process evaluation?

The word limit is **5000 words.**

- *The HRB encourages the development and application of agreed standardised sets of outcomes, known as 'core outcome sets', such as those reported by the COMET (Core Outcome Measures in Effectiveness Trials) Initiative.* ***Applicants must search the COMET database when considering which outcomes measures to include***[18]
- *You are advised to carefully address the potential benefits and difficulties presented by multi-site recruitment of patients or human subjects for the study in order to reach recruitment targets.*
- *Explain in detail how new techniques and/or or high-risk studies will be managed and suggest alternative approaches should these fail.*

[17] As appropriate, see J Cook et al. *DELTA2 guidance on choosing the target difference and undertaking and reporting the sample size calculation for a randomised controlled trial* https://www.bmj.com/content/363/bmj.k3750
[18] www.comet-initiative.org

- *Where new methods are being developed, arrangements for establishing validity and reliability should be described. Examples of non-standard questionnaires, tests, etc. should accompany the application or their content be clearly indicated.*
- *Useful links and resources are summarised in Appendix III.*

3.11 Participant flow diagram

Please upload a flow diagram showing the study design and the flow of participants. You should refer to the appropriate diagram depending on your study design (e.g. CONSORT for RCTs). Please see Appendix III for some useful links. This diagram should be submitted as a pdf and be clear as it will be referred to, and likely viewed on screen during the Panel discussion.

3.12 Discontinuation Criteria

Please specify appropriate "stopping rules" or discontinuation criteria for your study:

- For the individual participant
- For participating centres, which fail to include the estimated number of participants and
- For the whole trial

For example:
•Year 1 - expected recruitment = 50, discontinuation criteria = 5
•Year 3 - expected recruitment = 80, discontinuation criteria = 30
•Year 2 - expected number of participating centres = 5, discontinuation criteria = 2

It is not necessary to list discontinuation criteria for every KPI or milestone. Only the most fundamental to the success of the study as these will be reviewed as part of the post-award reporting and monitoring of successful awards by the HRB.
The word limit is **400 words.**

3.13 Internal Pilots

Are you planning to include an **Internal Pilot**? Internal pilots designed at the early stage of a definitive intervention trial can be included in the main study only where robust feasibility work has been completed and indicates that an internal pilot is appropriate. Details should be provided in the section "Evidence from previous feasibility studies".

Internal pilot studies designate a portion of the main trial as a pilot phase. At the end of the internal pilot study, the investigators re-compute preselected parameters and recalculate required sample size. The study then proceeds with the modifications dictated by the internal pilot. Final analyses of the results incorporate all data, disregarding the fact that part of the data came from a pilot phase. Those conducting pragmatic trials may wish to consult a published checklist to aid decision-making on whether pilot data can be carried forward to the main trial.[19]
The word limit is **500 words.**

[19] *G. Charlesworth et al. ACCEPT Acceptance checklist for clinical effectiveness pilot trials: a systematic approach. BMC Medical Research Methodology 2013 13:78*

3.14 Studies within a Trial (SWATs)

Are you planning to include a **Study Within a Trial** (SWATs)? SWATs should address an independent methodology research question on the design, conduct, analysis, reporting or dissemination of trials for which there is current uncertainty[20]. *Please see recently published guidance on how to decide whether a further SWAT is merited on the particular question*[21]. If yes, provide full details regarding the type of analysis to be undertaken, the rationale of the design proposed, the personnel who will conduct, power calculations, inclusion/exclusion criteria and costings as appropriate. Please clarify the relevance to and added value of the proposed SWAT to the main study.
An additional €20,000 in funding can be requested for conducting a SWAT. This is in addition to the €1,200,000 overall budget.

Support by the HRB-TMRN may be provided for DIFA2020 applications involving (SWATs). Check **https://www.hrb-tmrn.ie/support/grant-application-support/** for their specific deadlines in relation to support. Please see Appendix III for references on SWATs.
The word limit is **500 words.**

3.15 Public and Patient Involvement (PPI) in Research Project

The HRB promotes the active involvement of members of the public in the research that it funds where the HRB promote public and patient involvement (PPI) in the research that it funds where PPI contributors may include patients, potential patients, carers and people who use health and social care services as well as people from organisations that represent people who use services. HRB recognises that the nature and extent of active public and patient involvement is likely to vary depending on the context of each study.

Are you including public involvement in your application? YES/NO
If Yes, please describe (i) the purpose of the involvement, (ii) public and patient involvement to date and how that has influenced/changed what work has been planned, and (iii) public and patient involvement planned for the duration of the award (e.g. oversight, conduct, analysis and/or dissemination).

This section should be a summary of public and patient involvement activities. Please go into more details in other sections as appropriate. Provide information on the individuals/groups and the ways in which they will be involved.
If No, please explain why this is not applicable to your project.

Where members of the public/patients are involved, they must be compensated for their time and contributions; this should be reflected in the project budget.
*Please note PPI does **not** include the recruitment of study participants. Whilst this falls under patient-oriented research, it is participation of the public rather than involvement. It also does **not** include work aimed at raising awareness of the public around research, such as media publications of research findings, and outreach activities such as open days in research facilities.*
A number of useful links are included in Appendix III. The word limit is **500 words**.

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[20] S Treweek et al. *Trial Forge Guidance 1: what is a Study Within A Trial (SWAT)?* https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-018-2535-5
[21] S Treweek et al. *Trial Forge Guidance 2: how to decide if a further Study Within A Trial (SWAT) is needed* https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-019-3980-5

3.16 Impact statement

The statement should be as specific as possible and provide information that reviewers will find helpful in assessing the potential impact of the proposed research activity. An implementation plan that outlines the pathway to impact citing realistic timelines is requested.

Please provide details on the likely impact from the proposed research on patients, public and/or healthcare system and articulate the pathway by which the research will achieve this. By "Impact" we mean the direct contribution to improvements/benefits to patient care, health of the public and health services from this research in the short to medium term (1-5 years after the end of award). Where impact is mainly anticipated in an Irish context, please describe this for international reviewers and Panel members.

If you are proposing a feasibility study, please articulate the different expected impacts from the feasibility study, as well as the proposed future definitive intervention. The word limit is **500 words.**

3.17 FAIR data management and stewardship

The HRB's policy on management and sharing of research data[22] came into effect on 1st January 2020. In line with this policy, all **successful applicants will be required to submit a completed data management plan (DMP) to the HRB at the beginning of the study and a final updated version of the DMP with the final report at the end of the study.**

Describe the approach to data management and stewardship that will be taken during and after the project, including who will be responsible for data management and data stewardship. Please consider the FAIR Guiding Principles for scientific data management and stewardship: Findability, Accessibility, Interoperability, and Reusability[23].

With the support of data stewards or other data-related services support in your institution (typically library and ICT and digital services, etc) all Lead Applicants should address as much as possible the following regarding the management of the research data to be generated and/or re-used during the research study.

1. **Data description and collection or reuse of existing data**: (a) What is the type, format and volume of data? (b) How will the data be collected, created or reused?
2. **Documentation and data quality**: (a) What metadata and documentation will accompany the data (b) Will you make sure globally resolvable unique, persistent identifiers are in use (e.g DOI)?; what data quality control measure do you use?
3. **Storage and backup**: (a) How will data be stored and backed up during the research? (b) How will you manage data security and personal data protection?
4. **Ethical and legal compliance, codes of conduct**: (a) If personal data are involved, how will you manage compliance with legislation on personal data and security? (b) How will you manage legal issues, such as IPR, copyright, and ownership? Which legislation is applicable? (c) Which ethical issues and codes of conduct are there and how are they taken into account?

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[22] https://www.hrb.ie/funding/funding-schemes/before-you-apply/all-grant-policies/hrb-policy-on-management-and-sharing-of-research-data/

[23] Wilkinson, M. D. *et al.* The FAIR Guiding Principles for scientific data management and stewardship. *Sci. Data* 3:160018 doi: 10.1038/sdata.2016.18 (2016).

5. **Data sharing and long-term preservation:** (a) How and when will you share the data? (b) How do you select data for preservation and where data will be preserved long term (e.g. data repository, archive) (c) What methods or software tools are needed to access data? (d) Who will be responsible for data management (e.g. data steward), time needed for data management and for making data FAIR (costs should be added under the budget section, see Appendix V for further Guidance).

The word limit is **600 words**

3.18 IP considerations

The Lead Applicant together with the Host Institution has a duty to the public to ensure that discoveries and advancements in knowledge arising from any award are translated for public benefit including but not limited to commercial development of new therapies, diagnostics, materials, methodologies and software for health[24]. Please consult with the relevant Technology Transfer Office for advice on this section, where appropriate.

Please describe any current Intellectual property (IP) that will be relevant for the study and whether such IP assets are held by the applicants, and/or others outside the research team. Such IP might include software, checklists, scales, protocols, guidelines, questionnaires, or medicinal products for example. Has relevant background IP for your study been identified? If IP is required is there freedom to operate, such that this research can eventually be translated. What arrangements are in place to manage IP during the study, and ensure it is protected (if appropriate) prior to dissemination? Do you foresee any barriers to use of IP in order for the research outputs to be adopted?

The word limit is **500 words.**

3.19 Trial Management, Governance and Safety Monitoring

Arrangements for the management of the trials will vary according to the nature of the study proposed and should be proportionate to the complexity and associated risks. However, all should include an element of expert advice and monitoring that is **entirely independent** of the Lead Applicant, research team members and the institutions involved. Commonly, definitive trials are overseen by three committees: a Trial Management Group (TMG) a Trial Steering Committee (TSC) and an Independent Data Monitoring Committee (IDMC). Please refer to the description of the roles of the three Committees in Appendix IV of the Guidance notes.

Applicants are asked to submit their proposed arrangements for overseeing the trial and suggested membership for each of the committee(s):

- Describe the role of each team member (e.g. sponsor, principal applicant, coordinator, trial statistician, research personnel, collaborators, CRFs) in the day to day management of this study, for all aspects of the study including recruitment, randomisation, management and retention of biological samples, delivery of intervention, follow-up, data entry, quality assurance, data management and analysis.
- Describe the oversight, advisory or governance structures that will be established to oversee and monitor this trial; Trial Management Group (TMG) a Trial Steering Committee (TSC) and an Independent Data Monitoring Committee (IDMC)

[24] All HRB Host Institutions must subscribe to "Ireland's National IP Protocol 2019: A Framework for Successful Research Commercialisation" prepared by Government/Knowledge Transfer Ireland to ensure transparent and consistent procedures for managing Intellectual Property from publicly funded research.
https://www.knowledgetransferireland.com/Reports-Publications/Ireland-s-National-IP-Protocol-2019-.pdf

- Provide terms of reference for these groups and proposed membership
- Outline the processes that will be put in place to ensure that the trial is well managed, commenting on project management, meeting schedules, financial management and monitoring etc.
- If the study is multi-site, or multi-site and international please state any additional measures that will be undertaken to ensure the study is well managed.
- Please list anticipated risks to the successful delivery of the study and how it is planned to mitigate against those risks.
  The word limit is **2000 words**

3.20 Participants involved in trial delivery

Please list (where already known) any members of your proposed management, governance and safety committees as per the previous section. This section is not compulsory as we understand some of the positions may not have been populated yet. The maximum number of members you can add to each of these sections is highlighted in bold at the end of each line.

- Trial Sponsor – list if there is any additional trial sponsor/funder for this study. **(3)**
- Trial Management Group – see Appendix IV. **(10)**
- Trial Steering Committee – see Appendix IV. **(5)**
- Independent Data Monitoring Committee – see Appendix IV. **(10)**
- Trial Statistician – list the statistical expert(s) involved in any statistical analysis for the study. **(5)**
- Trial Supporting Facilities – list any infrastructures which may support the study. **(10)**
- Recruiting centres – list any sites that will be involved in recruitment of study participants (Sites within and outside Ireland). **(30)**
- Other participating groups/bodies – please list any additional affiliates of the study. **(10)**
- Review of trial protocol – Study protocols should be reviewed by an independent body to ensure an objective assessment/evaluation of the protocol prior to implementation. List the independent reviewer(s) of the trial protocol. **(5)**

3.21 Trial expertise in management, governance and safety committees

Does the research team include people with experience of successfully running large definitive trials?
Indicate trial expertise of all the above-mentioned participants by citing the 5 most relevant publications and/or specifying role in ongoing or previous trials(s) as appropriate. Ensure that the research team has the necessary expertise to carry out the study. The word limit is **500 words.**

3.22 Potential risk and ethical concerns

Please address any potential risk and/or harm to the safety of the patients or human subjects in the study, if relevant, and highlight any potential ethical concerns during this study and/or at follow up stage, even if not part of this application, and how you propose to deal with them. Does the proposed research include vulnerable groups; what additional considerations are there for these participants? The word limit is **500 words**.

3.23 Samples collection for Biobanking

Does your application include an element of biobanking? Y/N

Please describe how you will ensure good practice for biobanking components in this project, with particular regard to quality of sample collection, processing, annotation and storage, and describing data protection measures where appropriate. Please reference relevant guidelines/standards you will use.
The word limit is **250 words.**

3.24 Sex and/or Gender issues in the research study

Are there potential sex (biological) considerations for this study?

Are there potential gender (socio-cultural) considerations for this study?

- If so, outline how sex and/or gender analysis will be integrated in the design, implementation, evaluation, interpretation and dissemination of the results of the research proposal.
- If not, you must clearly demonstrate why it is not relevant to the research proposal; have you done a literature search to confirm this?

Please see Appendix III for resources on gender and sex considerations in research proposals.
Please note this section is intended to focus researchers on the research content, and not the gender balance within the research team.
The word limit is **500 words.**

3.25 Dissemination and Knowledge Exchange Plan

Please note: *HRB requires that all HRB-funded interventions to be registered in a publicly accessible register prior to initiation of the study. Results must be reported on the register within twelve months of completion of the intervention.*

Include a clear dissemination and knowledge exchange plan to indicate how the research outputs you anticipate producing during and after your study will be disseminated and shared and made openly accessible, in line with HRB Open Access Policy[25]. Outputs may include research articles, research data, datasets, software code, clinical guidelines, nanopublications[26], educational resources, reports, policy briefs and other relevant documents. Protection of Intellectual Property should be considered before data are disseminated[27].

Who are the various audiences and communities that need to be targeted if these results are to have any impact? What is your dissemination plan to address this? Describe academic publication plans and/or plans for technology transfer. Describe how the findings of this research will be publicised to the HSE or wider health community in a manner that will optimise impact on health policy and/or practice? If possible, reference should be made to any aspects of the study which may be undertaken to ensure adoption beyond the term of the award.

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[25] http://www.hrb.ie/research-strategy-funding/policies-and-guidelines/policies/open-access/
[26] A nanopublication is the smallest unit of publishable information: an assertion about anything that can be uniquely identified and attributed to its author **http://nanopub.org/wordpress/**
[27] All HRB Host Institutions must subscribe to the National Intellectual Property Protocol, '**Inspiring Partnership- the national IP Protocol 2016: Policies and resources to help industry make good use of public research in Ireland**', prepared by Government/Knowledge Transfer Ireland to ensure transparent and consistent procedures for managing Intellectual Property from publicly funded research.

Please note the HRB has a mandatory Open Access publication policy; demonstrate how you plan to make all publications open access. Types of publication routes include [28]:

- **Green Route:** publishing in a traditional subscription journal. Articles are 'self-archived' (added) to a repository (institutional or external subject-based) and usually made available after an embargo period, which is set by the publisher.
- **Gold Route:** publishing in an open access or hybrid journal. Articles processing charges (APCs) are required so that the article is openly available immediately on publication and can be added to a repository (institutional or external subject-based).

HRB Open Research: rapid open peer reviewed and open access platform for all research outputs, with all publication charges covered centrally by the HRB at no expense to the grantee. (**www.hrbopenresearch.org**)

The word limit is **600 words**.

3.26 Communication with Research Participants

Briefly describe how you plan to communicate with research participants during the study, and once results of the study are known. Please give details of how you plan to do this, who will communicate with participants, and at what intervals communication will occur.

The word limit is **200 words**.

3.27 Study Description Uploads

A file upload option is available to include an attachment to support your Study Description. A maximum of 5 figures, which can be a combination of images, logic model diagrams, graphs, tables, scales, instruments or surveys, may be uploaded as a **single document** on HRB GEMs. They must not be embedded within the text of the Project Description. The maximum size is **10MB.** Additionally, a draft protocol can be uploaded, if available.

3.28 References

A full description of the Publications cited in the Project Description should be provided. You can enter a maximum of 30 publications. Please enter references in the same format. For example, the following format may be used:

Gallagher PA, Shoemaker JA, Wei X, Brockhoff-Schwegel CA, Creed JT. Extraction and detection of arsenicals in seaweed via accelerated solvent extraction with ion chromatographic separation and ICP-MS detection. Fresenius J Anal Chem. 2001 Jan 1;369 (1):71-80. PMID: 11210234.

For book and printed source citations:

Farrell M, Gerada C and Marsden J (2000) *External review of drug services for the Eastern Health Board.* London: National Addiction Centre.

[28] Source: https://www.jisc.ac.uk/guides/an-introduction-to-open-access

4.0 Details of Research Team

For applications utilising the option of two Co-Lead Applicants, information will be requested for each person. Please give high-level details as part of the role description as to how the roles will differ between the two Co-Leads.

Please note, this option is only available where at least one of the Co-Leads is a Health and Care Practitioner researcher practising in Ireland.

4.1 Expertise of Research Team

Show how the team has the collective expertise, competencies and experience to successfully deliver this particular study, under the leadership of the Lead Applicant. In particular consider whether adequate research design methodological expertise including statistical expertise been sought and incorporated within the team. Mention and justify any changes to the research team from Pre-Application stage, if applicable. The word limit is **500 words**.

4.2 Lead Applicant's Role

Firstly, please indicate the **current commitment** to research/clinical/teaching/other, either as a percentage or a proportion of a full time equivalent (FTE). Give an outline of the role of the Lead Applicant in this study on a day-to-day basis. Please indicate below the proposed amount of time to be dedicated to working on **this study**, either as a percentage or a proportion of a full time equivalent (FTE). The word limit is **250 words**.

4.3 Co-Lead Applicant's Role (if applicable)

Give an outline of the role of the Co-Lead Applicant in this project on a day-to-day basis including the amount of time to be dedicated to working on this study, either as a percentage or a proportion of a full time equivalent (FTE).

The word limit is **100 words**.

4.4 Co-Applicant's Role

Give an outline of the role of all Co-Applicants in this project on a day-to-day basis including the amount of time to be dedicated to working on this project either as a percentage or as a proportion of a full time equivalent (FTE). The word limit is **250 words**.

4.5 Collaborator's Role

Include details of all collaborators involved in the project and state their contribution to the project.

The word limit is **100 words**.

4.6 Personnel

List all personnel to be funded through this study and describe what aspects of the proposed research they will be involved in.

4.7 Personnel Justification

Give a brief justification for requested personnel relative to the scale and complexity of the research study. *NOTE this scheme is **not framed as a training initiative**. The required expertise, risks and dependencies inherent in clinical trials do not align well with the needs of those registered for a higher degree. Thus, **no PhDs** are funded through this scheme*.

The word limit is **250 words.**

5.0 Infrastructure and Support

5.1 Infrastructure and Support

Describe the infrastructure, facilities, specialist expertise and other support available at the Host Institution and/or at other sites where the research will be conducted. Please include details of critical supports in areas such as statistics, methods, trial management or regulatory expertise where this is being provided above and beyond the activities/expertise of members of the research team.
The word limit is **400 words.**

5.2 Access to a Clinical Research Infrastructure

Applicants are expected to avail of the advice, trial and data management services and/or other forms of support from existing research infrastructures such as a Clinical Research Facility/Centre (CRF/CRC), Centre for Applied Medical Imaging (CAMI), HRB Clinical Research Co-ordination Ireland (HRB CRCI), the HRB Trials Methodology Research Network (HRB TMRN[29]) and/or a thematic HRB Clinical Trials Network (HRB CTN). Applicants are requested to provide an overview detailing the scope and nature of the engagement (this includes national facilities and/or international facilities and Units/networks as appropriate to the proposed study).

Applicants need to provide an **Infrastructure Agreement form** (including national and international infrastructures as required) setting out the following information:

- Name and address of the infrastructure
- Web links
- Information on the nature and stage/s of the input/advice/collaboration/service
- Rationale for the choice of infrastructure
- Information on the costs of providing the service/input, setting out where this is provided in-kind, from additional funding or requested from the project budget
- Any issues related to feasibility

An Infrastructure Agreement Form can be downloaded from the Infrastructure and Support page of this GEMs application and must be completed for each support service involved. The Form must be completed, signed, dated and uploaded on GEMs. Electronic signatures are acceptable for letters/forms that are uploaded on GEMs. **Applicants must take note of the individual deadlines for application for support from the various infrastructures and contacting these infrastructures should be done as early as possible to avoid capacity issues.**

Note: Applications which do not detail such input, advice and/or support (and where this expertise is not clearly evident within the applicant team) should justify why they have chosen not to access such support.

[29] Support by the HRB-TMRN requires the inclusion of a primary methodological study within a trial (SWAT) or must include a non-standard novel trial design

6.0 Budget

Please note that the budget section will not be pre-populated with the indicative budget in the Pre-Application. Please take into account any changes to personnel costs, e.g. arising as a result of National Pay Agreements. Please ensure you have reviewed the HRB-CRCI checklist for guidance for costs, and that you liaise at an early stage with your Host Institution to ensure that you have appropriately captured costs, in particular related to sponsorship.

Please provide a summary and justification of the costs and duration associated with the project.
The maximum total value of an award is €1,200,000 inclusive of overhead contribution. An additional €20,000 (inclusive of overheads) can be applied for if conducting a SWAT study[30]. **There is no set limit per annum** therefore the proposed budget per annum should reflect anticipated annual costs.

The budget requested and award duration must reflect the scale and nature of the proposed research and reviewers will thoroughly assess the level of funds and timeframe requested when reviewing the proposal.

Please note: salaries should be commensurate with experience. HRB does not expect salaries in excess of IUA Level 3 for trial coordinator/project manager. A higher salary may be allowable for international trials; this would need to be justified in the context of the specific trial, and of the proposed role of the salaried person.

A **full detailed breakdown** of **costings** and **justification for all funding** is required for items listed under each subheading. You are strongly advised to seek guidance from the research office/finance office in the host institution before completing this section of the form. Please refer to the HRB-CRCI checklist **https://www.hrb-crci.ie/** for guidance on clinical trial costs. **Please note that some costs listed in the HRB-CRCI checklist are not eligible for HRB funding (e.g. salary or benefits of academic staff within research institutions that are already in receipt of salary or benefits. The HRB does not provide salary or buy out time for collaborators.)**

The HRB will not provide additional funding in the case of either under-estimates or over expenditure.
Funds will be provided for the following:

1. Personnel costs	Must be listed for each salaried personnel under each of the following subheadings (a-c):
a) Salary	Gross Annual Salary (including 5% employee pension contribution) negotiated and agreed with host institution. Applicants should use the IUA website scales for the most up-to-date recommended salary scales for academic researchers **http://www.iua.ie/research-innovation/researcher-salary-scales/** Please note employee pension contribution of 5% has already been incorporated into the IUA gross salary figure.

[30] Please note that individual proposed SWATs may cost more or less than €20,000; actual costs should be included. The additional budget allowance for SWATs is to encourage and support further SWATs within the HRB-funded portfolio.

	Applicants are advised that public sector pay increases for the period until end of 2020 have been agreed. Please find new pay scales at **https://www.iua.ie/research-innovation/researcher-salary-scales/** If your application stretches beyond 2020; please apply a salary contingency of 2.5% p.a. **Applicants should include annual pay increments for staff and related costs (pension contribution, employer's PRSI contribution, and overhead contribution) in the budget.** **Note:** The HRB does not provide funding for the salary or benefits of academic staff within research institutions that are already in receipt of salary or benefits. The HRB does not provide salary or buy out time for collaborators
b) Employer's PRSI	Employer's PRSI contribution is calculated at 11.05% for 2020
c) Employer Pension Contribution	Pension provision up to a maximum of 20% of gross salary will be paid to the host institution to enable compliance with the Employment Control Framework (an additional 5% employee contribution is part of the salary). The level of employer contribution should be in accordance with the model adopted by the host institution. If applicable, state the amount of employer contribution based on the pro rata salary and note the % of pro rata salary used to calculate this for reference. Circular Letter 6/2007 states that the pensions contribution of all Public Health Service employees who, on or after 1 June 2007, are granted secondments or periods of special leave with pay to enable them take up appointments with other organisations, including other Public Health Sector organisations, will be increased to 25% of gross pensionable pay. The rate of 25% of gross pensionable pay referred to in this context is the pension contributions to be paid by the body to which the employee is seconded – it does not include any pension contributions which employees make themselves. Where no such arrangements are in place, the HRB will not be liable for costs. If requesting pension costs linked to Circular 6/2007, please provide details as justification for the request.
2. Running Costs	For all costs required to carry out the research including materials and consumables, survey costs, travel for participants, transcription costs, trial-specific training for personnel etc. Please consult with your Host Institution in relation to trial-related insurance costs. Access to necessary special facilities or services which are not available in the host academic or clinical institutions. i.e., consultancy fees, methodological support, Clinical Research Facilities support, MRI facilities etc. will be considered under running costs as long as they are detailed in an accompanying 'Infrastructure Agreement Form'.

	Costs associated with involving members of the **public or patients** in your research e.g. consultation workshops, costs of participation in advisory groups, travel expenses, honoraria, etc. should be charged to running costs. The following costs are ineligible and will not be funded: animal study costs, inflationary increases, cost of electronic journals. Note: Please see a list of costs that fall within the overhead contribution below and which should not be listed under running costs.
3. Equipment	Funding for suitably justified equipment can be included in this section. Personal/Stand-alone computers will not be funded. All costs must be inclusive of VAT, where applicable.
4. Dissemination Costs	Costs associated with publication of results, seminar/conference attendance (provide details of name and location, where possible) and any other means of communicating/reporting research outcomes as detailed in the dissemination and knowledge exchange plan. Data sharing costs can be included here. Please refer to the HRB policy on Open Access to Published Research[31]. Please list dissemination costs under the following categories: publications, conferences, other activities. **Publications:** Typically, the average HRB contribution towards publication costs is €1,750/per article or **HRB Open Research:** rapid open peer reviewed and open access platform for all research outputs, with all publication charges covered centrally by the HRB at no expense to the grantee. (**www.hrbopenresearch.org**) **free of charge**. **Conferences:** We envisage that conference costs will be typically around €500 per national conference and €1,500 per international conference.
5. FAIR data Management and Stewardship	Costs related to data management, FAIRification, storage and archiving of research data in line with best practice of data management and stewardship and the FAIR principles **incurred during the lifetime of the study** should be included. Cost of data management support calculated by hourly rates should also be included here. Please consult Appendix V of the Guidance Notes for examples of eligible costs.
6.Overhead Contribution	In accordance with the HRB Policy on Overhead Usage, the HRB will contribute to the indirect costs of the research through an overhead payment of 30% of Total Direct Modified Costs (TDMC excludes student fees, equipment and capital building costs)

[31] http://www.hrb.ie/research-strategy-funding/policies-and-guidelines/policies/open-access/

	for **laboratory or clinically based research** and 25% of Total Direct Modified Costs for desk based research. The following items are included in the overhead contribution: personnel recruitment costs, bench fees, office space, software, contribution to gases, bacteriological media preparation fees, waste fees, bioinformatics access.

6.1 Use of resources

Please demonstrate that the resources requested, plus other in-kind resources where applicable, are sufficient to successfully deliver this study, to target and on time. Please explain how good use is made of the budget requested, sharing resources where it is appropriate. The reviewers will carefully assess costs within the HRB budget for e.g. drugs or devices to be used, so this should be justified in this section.
The word limit is **200 words**.

7.0 History of Application and Other Funding

7.1 History of the application (if applicable)

Please indicate whether this or a similar application has previously been submitted to the Health Research Board in the last three years. If yes, what year and scheme? Briefly describe the changes that have been made to the application. Have the recommendations from any previous peer, panel or public review you received influenced the changes you have made? In instances where your previous proposal was funded, please outline how it contributed to the progression of this research. Where supplemental funding is sought, the rationale for this needs to be clearly articulated and well justified. The word limit is **200 words**.

7.2 Other Funding Sources

Please indicate if you have submitted this, or a similar application, to another funding body previously. Please indicate which funding body, project title, result of submission or when outcome is expected and the amount of award.

7.3 Other Financial Support

Give details of any other financial support or in-kind support available for this or any other related project e.g. existing national or international studies or co-funding from partner organisations. Indicate project title, funding agency, partner organisation or sponsor and the amount of award/co-funding. Failure to disclose accurately or fully may result in your application being deemed ineligible and withdrawn without further review.

8.0 Ethical Approval, Clinical Trial Approval and Sponsorship

8.1 Ethical Approval

Ethical approval is required for all research work funded by the HRB that involves human participants. In addition, Clinical Trial Approval from the Health Products Regulatory Authority is required for trials involving medicinal products.

8.2 Clinical Trial Approval details

The Sponsorship responsibilities for Clinical Trials of Investigational Medicinal Products (CTIMPs) are governed by the EU Clinical Trial Regulation EU#536/2014. The Sponsorship responsibilities for Clinical Investigation of a Medical Device are governed by the EU Medical Device Regulation 2017/745. For reference to current legislation please visit the HPRA website. Applicants are responsible for ensuring that all necessary approvals are in place prior to the start of the research.

8.3 Letter of Sponsorship Upload

Please review the HRB Clinical Trials and Interventions Research Governance Policy[32]. Please note that all trials (Regulated and non-Regulated) directly funded by HRB will require a sponsor (as defined in the policy). *The HRB cannot act as the sponsor.* The sponsor for HRB-funded trials cannot be an individual or company.

Sponsorship oversight should be planned and put in place for the duration of the clinical trial. The level of oversight required during the implementation of the clinical trial should be assessed carefully and commensurate with the clinical trials risk level. All clinical trials and interventions must undergo a risk assessment (at the Host Institution level) before an application is submitted to support the sponsorship decision and oversight arrangements required[33]. *Lead Applicants should engage with their Host Institution as soon as they are invited to submit a Full Application to ensure sufficient time for this process.*

Please **upload a signed document**, on headed paper from the agreed sponsor. This **Letter of Sponsorship** must (a) confirm willingness to take on the role of the sponsor as defined in the HRB Clinical Trials and Interventions Research Governance Policy, and include details on (b) sponsor responsibilities for the study, (c) any responsibilities delegated to third parties and (d) confirming that the study will be conducted in compliance with Irish and European legislation and guidance and in accordance with the ethical and scientific principles of the Declaration of Helsinki and ICH guidelines.

[32] https://www.hrb.ie/funding/funding-schemes/before-you-apply/all-grant-policies/hrb-policy-on-clinical-trials-and-interventions-governance/

[33] Many HRB Host Institutions contributed to the **Corporate Enabling of Clinical Research** initiative, which included work on common approaches to institutional risk assessments before taking on the role of clinical trial sponsor. For more information see the full 2019 report at **https://crdi.ie/corporate-enabling-of-clinical-research/**, and contact your Host Institution in relation to their specific requirements

9.0 Submission of Full Applications

The deadline for submission of complete Full Applications will be 13:00 on 7th July 2020[34]

1. After successful validation the Lead Applicant may submit the application. It will then be routed to the designated signatory at the Host Institution for their approval.
2. If a signatory rejects the application the Lead Applicant will be notified, along with any feedback the signatory has supplied.
3. The application can then be re-submitted; it will be returned to the signatory and will continue through the approval process as before.
4. On completion of the final approval by the Host Institution signatory, a grant application number is assigned to the application.
5. The application automatically gets submitted to the HRB through GEMs for consideration for funding.

Please note that the HRB will not follow up any supporting documentation related to the application, such as Host Institution's Letters of Support, Collaborator Agreement Form, Gantt charts etc. It is the responsibility of the Lead Applicant to upload all supporting documentation prior to submission. If the documentation is not received by the HRB on time, in the correct format or is not properly signed or submitted, the application will be deemed ineligible without further review.

The HRB reserves the right to reject any application that does not meet the terms of this call. The HRB's procedure for appealing funding decisions is available at http://www.hrb.ie/research-strategy-funding/policies-guidelines-and-grant-conditions/policies-and-position-statements/

[34] The deadline for Full Applications will be kept under review, depending how the situation with Covid-19 evolves in Ireland

Appendix II: Checklist for Intervention studies (randomised and non-randomised designs)

Regardless of whether your project involves an evaluation of a simple or a complex intervention and regardless of whether it is based on a randomised or a non-randomised design, the review Panels will take into account the following key questions when assessing the application. It is recommended that you use this checklist as a guide before finalising and submitting your application. It is also recommended that you seek advice from individuals or centres that are experts in study design and statistics before submitting your application.

The need for the study

- What is the problem to be addressed?
- What is/are the principal research question(s) to be addressed?
- Does your intervention have a coherent theoretical basis?
- Does the existing evidence – ideally collated from systematic reviews – suggest that it is likely to be effective or cost effective?
- What outcome are you aiming for and how might this bring about change?
- Can it be implemented in a research setting?
- Describe any risks to the safety of participants involved in the trial

The Proposed Study

- Is this a definitive trial or a feasibility study? If a feasibility study, state explicitly the type of feasibility (see *Eldridge et al 2016*)
- What is the proposed study design? e.g. randomised or non-randomised, experimental or observation design, pragmatic or equivalence, conventional parallel group RCT as opposed to cluster, factorial or stepped-wedge design etc.
- What are the planned interventions?
- Have you fully described 'usual care'?
- Indicate the number of subjects to be enrolled (both active treatment and controls)
- What are the proposed practical arrangements for allocating participants to study groups? E.g. Randomization method. If stratification or minimization are to be used, give reasons and factors to be included.
- What are the proposed methods for protecting against sources of bias? e.g. Blinding or masking. If blinding is not possible please explain why and give details of alternative methods proposed, or implications for interpretation of the trial's results
- How variable is the intervention (between sites, over time etc.)?
- Have you adequately described the context and the environment in which the evaluation is being undertaken?
- What are the planned inclusion/exclusion criteria?
- What is the proposed duration of intervention period?
- What is the proposed frequency and duration of follow up?
- Have you discussed reliability and validity of all study instruments or scales?

- What are the proposed primary and secondary outcome measures?
- How will the outcome measures be measured at follow up?
- Will health service research issues be addressed? Justify inclusion/exclusion of health economics and quality of life measures. If these measures are to be included full details should be given including power calculations.
- What is the proposed sample size and what is the justification for the assumptions underlying the power calculations? Include for both control and intervention groups, a brief description of the power calculations detailing the outcome measures on which these have been based, and give event rates, means and medians etc. as appropriate.
- It is important to give the justification for the size of the difference that the trial is powered to detect. Does the sample size calculation take into account the anticipated rates of non-compliance and loss to follow-up given below?
- What is the planned recruitment rate? How will the recruitment be organised? Over what time period will recruitment take place? What evidence is there that the planned recruitment rate is achievable?
- Are there likely to be any problems with compliance? On what evidence are the compliance figures based?
- What is the likely rate of loss to follow up? On what evidence is the loss to follow-up rate based?
- How many centres will be involved?
- Has any pilot or feasibility work been conducted to be confident that the intervention can be implemented as intended?
- Has acceptability testing been considered? What user involvement is there in the study?
- Is your study ethical?
- Are there any local or other contextual issues that need to be factored into the design?

Data Collection and Management

- What are the arrangements for day to day management of the trial? e.g. Randomisation, data handling, and who will be responsible for coordination?
- What arrangements have you put in place to oversee and monitor the evaluation?
- Is there a need for a trial steering Panel or a data safety and monitoring Panel?
- What is the proposed type of analyses?
- What is the proposed frequency of analyses?
- Are there any planned subgroup analyses?
- Will the design chosen really enable you to draw conclusions about effectiveness?

Appendix III: References/Useful Links

Study design for interventions

- **"Defining Feasibility and Pilot Studies in Preparation for Randomised Controlled Trials: Development of a Conceptual Framework"** by Eldridge S. *et al.* **http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0150205**

- **"The PRECIS-2 tool: designing trials that are fit for purpose"** by Louden *et al.* **http://dx.doi.org/10.1136/bmj.h2147**

- **"A process for Decision-making after Pilot and feasibility Trials (ADePT): development following a feasibility study of a complex intervention for pelvic organ prolapse"** by Bugge C *et al*. **http://trialsjournal.biomedcentral.com/articles/10.1186/1745-6215-14-353**

- **"Developing and Evaluating Complex Interventions"** by MRC, UK **www.mrc.ac.uk/complexinterventionsguidance**

- **"Process evaluation of complex interventions: Medical Research Council guidance" by Moore GF. e*t al.*** **http://dx.doi.org/10.1136/bmj.h1258**

- **"Using natural experiments to evaluate population health interventions**: **Guidance for producers and users of research evidence"** by MRC, UK **www.mrc.ac.uk/naturalexperimentsguidance**

- **Consort 2010 Statement**: updated guidelines for reporting parallel group randomised trials **www.consort-statement.org**

- **SQUIRE Guidelines**: provides a framework that authors can use when developing proposals or writing research articles about quality improvement **www.squire-statement.org**

- **HIQA Guidelines** for the Economic Evaluation of Health Technologies in Ireland (2018) **https://www.hiqa.ie/reports-and-publications/health-technology-assessment/guidelines-economic-evaluation-health**

- **HIQA Guidelines** for the budget Impact Analysis of Health Technologies in Ireland (2015) **https://www.hiqa.ie/system/files/Guidance_on_Budget_Impact_Analysis_of_Health_Technologies_in_Ireland.pdf**

- **HIQA Guidelines** for Evaluating the Clinical Effectiveness of Health technologies in Ireland (2011) **http://www.hiqa.ie/system/files/HTA-Clinical-Effectiveness-Guidelines.pdf**

Studies within a Trial (SWATs)

- **Expert support for developing SWATs (check their deadlines)**
  www.hrb-tmrn.ie

- **What is a SWAT**
  https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-018-2535-5

- **How to decide if a particular SWAT is needed**
  https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-019-3980-5

- **SWAT repository**
  http://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/SWATSWARInformation/Repositories/SWATStore/

Study registration

- **International Clinical Trials Registration Platform** (run by the WHO)
  http://apps.who.int/trialsearch/Default.aspx

- **European Clinical Trials Database** (EudraCT): database of all regulated clinical trials which commenced in the EU from 1 May 2004
  https://eudract.ema.europa.eu/results-web/

- **US National Library of Medicine database:** database of privately and publicly funded clinical studies – regulated and unregulated - conducted around the world
  https://www.clinicaltrials.gov/

Reporting

- **COMET (Core Outcome Measures in Effectiveness Trials) Initiative**: development and application of agreed standardised sets of outcomes, known as 'core outcome sets'
  http://www.comet-initiative.org/

- **EQUATOR Network Library for health research reporting**: an international initiative that seeks to improve reliability and value of health research literature by promoting transparent and accurate reporting of research studies
  https://www.equator-network.org/library/

- **Registry of Research Data Repositories**
  http://www.re3data.org/

- **Zenodo Data Repository (OpenAIR)**
  https://zenodo.org/about

Clinical Research Infrastructures

- **Health Research Board Trials Methodology Research Network (TMRN)**
  https://www.hrb-tmrn.ie/

- **HRB Clinical Research co-ordination Ireland (HRB CRCI)**
  https://www.hrb-crci.ie/

- **HRB Critical Care Clinical Trials Network Ireland (HRB Critical Care CTNI)**
  https://www.hrb-crci.ie/clinical-research-networks/

- **HRB Mother & Baby Clinical Trials Network Ireland (HRB Mother & Baby CTNI)**
  https://www.hrb-crci.ie/clinical-research-networks/

- **HRB Primary Care Clinical Trial Network Ireland (HRB Primary Care CTNI)**
  https://www.hrb-crci.ie/clinical-research-networks/
  http://primarycaretrials.ie/

- **HRB Stroke Clinical Trial Network Ireland (HRB Stroke CTNI)**
  https://www.hrb-crci.ie/clinical-research-networks/

- **Health Research Board Clinical Research Facility, Galway (HRB CRFG)**
  http://www.nuigalway.ie/hrb_crfg/

- **Health Research Board Clinical Research Facility, Cork (HRB CRFC)**
  http://www.ucc.ie/en/crfc/

- **Wellcome Trust-Health Research Board Clinical Research Facility, St James's Hospital (WT-HRB CRF SJH)**
  http://www.sjhcrf.ie/

- **Clinical Research Facility, University College Dublin**
  http://www.ucd.ie/medicine/ourresearch/researchcentres/ucdclinicalresearchcentre/

- **Clinical Research Centre, Royal College of Surgeons in Ireland**
  http://www.rcsi.ie/index.jsp?p=331&n=696

- **Health Research Institute Clinical Research Support Unit Limerick**
  https://www.ul.ie/hri/clinical-research-support-unit

- **Children's Clinical Research Unit, CHI Crumlin**
  https://www.nationalchildrensresearchcentre.ie/childrens-clinical-research-unit/

- **Centre for Advanced Medical Imaging, St James' Hospital Dublin**
  http://www.3tcentre.com/

Public and Patient Involvement

- **Public Involvement Impact Assessment Framework:** Provides tools for successful involvement of members of the public in research projects and for assessment of impacts
  http://piiaf.org.uk/

- **PPI cost calculator**
  http://www.invo.org.uk/resource-centre/payment-and-recognition-for-public-involvement/involvement-cost-calculator/

- **European Patient Forum Value + Handbook:** For Project Co-ordinators, Leaders and Promoters On Meaningful Patient Involvement
  http://www.eu-patient.eu/globalassets/projects/valueplus/doc_epf_handbook.pdf

- **The James Lind Alliance Priority Setting Partnerships:** Research priorities in disease areas set jointly by patients, clinicians and researchers
  http://www.jla.nihr.ac.uk/

- **INVOLVE UK website for resources on Public and Patient Involvement in research**
  http://www.invo.org.uk

- **How to involve people in research**
  http://www.invo.org.uk/find-out-more/how-to-involve-people/

Biobanking

- **OECD Guidelines on Human Biobanks and Genetic Research Databases**
  http://www.oecd.org/science/biotech/44054609.pdf

- **ISBER Best Practices for Repositories**
  http://www.isber.org/?page=BPR

- **Molecular Medicine Ireland Biobanking Guidelines**
  https://www.crdi.ie/resources/biobanking-guidelines/

- **NCI Best Practices for Biospecimen Resources (2016)**
  https://biospecimens.cancer.gov/bestpractices/2016-NCIBestPractices.pdf

Data management and sharing and FAIR principles

- **Digital Curation Centre: How to develop a data management and sharing plan and examples DMPs**
  http://www.dcc.ac.uk/resources/data-management-plans/guidance-examples

- **FAIR data principles FORCE 11**
  https://www.force11.org/fairprinciples

- **UK Concordat on Open Research Data (July 2016)**
  http://www.rcuk.ac.uk/documents/documents/concordatopenresearchdata-pdf/

- **Guidelines on FAIR data management plans in Horizon 2020**
  http://ec.europa.eu/research/participants/data/ref/h2020/grants_manual/hi/oa_pilot/h2020-hi-oa-data-mgt_en.pdf

- **FAIR at the Dutch centre for Life sciences**
  https://www.dtls.nl/fair-data/

- **Registry of Research Data Repositories**
  http://www.re3data.org/

Gender issues in research

- **Examples of case studies in Health & Medicine where gender/sex in research matters**
  http://genderedinnovations.stanford.edu/case-studies-medicine.html

- **Gender Toolkit in EU-funded research for examples and guidance**
  http://www.yellowwindow.be/genderinresearch/downloads/YW2009_GenderToolKit_Module1.pdf

Evidence synthesis

- **The Cochrane Library:** online collection of databases in medicine and other healthcare specialties which summarise and interpret the results of medical research.
  www.thecochranelibrary.com

- **The Campbell Collaboration:** promotes positive social and economic change through the production and use of systematic reviews and other evidence synthesis for evidence-based policy and practice
  https://www.campbellcollaboration.org/

- **The Campbell Collaboration UK & Ireland**: hub at Queens University Belfast
  https://www.qub.ac.uk/research-centres/CampbellUKIreland/

Appendix IV: Trial Oversight Committees

Trial Management Group (TMG)

The TMG oversees the day-to-day management and overall conduct and progress of the trial. The group normally includes the Chief Investigator(s), Trial Manager, Statistician and Data Manager. In addition, the group may include other members of the trial team with specific expertise, such as the Database Programmer, Pharmacist, Health Economist and one or two site Principal Investigators.

Group meetings are essential to keep members up to date with the trial and to monitor progress. The frequency of meetings is trial dependent; however, it is recommended that this group would meet frequently during trial set-up and at least quarterly thereafter. A meeting should also be held before a TSC meeting to plan the agenda and required meeting papers.

Trial Steering Committee (TSC)

The role of the TSC is to provide oversight of the trial on behalf of the sponsor and funder and ensure that the trial is conducted in accordance with the principles of GCP and relevant regulations. The TSC should focus on the progress of the trial, adherence to the protocol and participant safety. In addition, the TSC should review any relevant new information regarding the intervention or clinical area that may impact on the trial.

The terms of reference should be agreed at the start of the first meeting of the committee. It is recommended that a TSC includes an independent Chair, has a majority of independent voting members and includes a public/patient representative. The non-independent members would normally include the Chief Investigator and one or two other investigators. Representatives from the sponsor and/or funder may be invited to meetings. Relevant members of the TMG should attend committee meetings to present information as required.

Independent Data Monitoring Committee (IDMC)

The role of the DMC is to monitor data emerging from the trial, in particular in relation to safety and efficacy, and make recommendations to the TSC regarding any safety issues that should be brought to the attention of participants or any ethical reasons why the trial should not continue. Usually the DMC is the only group to have access to unblinded data during the course of the trial. In addition, it considers whether or not any interim analyses are required and would review these data. All members should be **totally independent** of the trial. The DMC is usually made up of three or four members and includes an independent chair and experts in the field such as clinicians with expertise in the relevant area and expert statisticians. **Trial Statisticians usually attend meetings and present the data**. The Chair will report his or her recommendations to the Chair of the TSC.

The DMC terms of reference, or charter, should be agreed before the start of the trial. This document will outline any **stopping rules** and the frequency of interim data analyses during the recruitment phase of the trial.

It is expected that nearly all randomised controlled trials (RCTs) will have a DMC; however, for relatively small and/or low risk trials, the TSC may also assume this role. The TSC or the funder and/or sponsor may decide this. Meetings are usually held annually; however, the DMC can meet more frequently if necessary.

Appendix V: FAIR Data Management

Introduction

For researchers, the move to FAIR and open[35] data, where possible, means that they have the responsibility to think about what data their research will produce, how these data will be described, and how they can be made available in such a way so as to benefit science and society in general. This means that they have to draw up a data management plan (in collaboration with professionally trained colleagues) and find suitable data repositories at a very early stage of their research. FAIR principles should be applied to all research involving data and/or software creation and so be included in all data management plans (DMPs). The DMP is not be a goal in itself and should not be regarded as an additional administrative hurdle. It should instead provide an opportunity at an early stage of the research project to consider how the data generated within a project will be stored, managed and safeguarded, and thus be part of the research process from the outset. As a project progresses, the data generated may well change in type and volume, so the DMP should be seen as a dynamic framework which should be maintained and modified as the research advances.

DMP Requirements

The HRB's policy on management and sharing of research data[36] came into effect on 1st January 2020. In line with this policy, all **successful applicants will be required to submit a completed data management plan (DMP) to the HRB at the beginning of the study and a final updated version of the DMP with the final report at the end of the study.** The DMP will need to be submitted alongside a certification of approval from the designated representative(s) within the Host Institution. Successful applicants will be expected to use the HRB Data Management Plan template available through DMPOnline - **https://dmponline.dcc.ac.uk/**
The requirements of the HRB's DMP template can be found here **https://dmponline.dcc.ac.uk/template_export/1814665590.pdf**

FAIR Data Management Costs

Examples of FAIR Data Management **Costs** are listed in the table below. Costs related to management, FAIRification, storage and archiving of research data (as part of the DMP pilot the HRB is currently conducting) in line with best practice of data management and stewardship and the FAIR principles. Some of the eligible costs may include:

People	Staff time per hour for data collection, data anonymisation,
	staff time per hour for data management/stewardship support, training, etc
Storage and computation	cloud storage, domain hosting charge
Data access	secondary data access, costs for preparing data for sharing (eg anonymisation)

[35] *Please note that not all FAIR data are necessarily open. Where data raises data protection or security concerns, controls and limits on data access will be required. In some cases, it will be appropriate for researchers to delay or limit access to data in order to secure intellectual property protection. Any such restrictions on access should be justified, made explicit via machine-actionable licensing and built-in accessibility protocols mechanisms.*
[36] https://www.hrb.ie/funding/funding-schemes/before-you-apply/all-grant-policies/hrb-policy-on-management-and-sharing-of-research-data/

Deposition and reuse	costs for depositing research data and metadata in an open access data repository
	e.g. defining semantic models, making data linkable, choosing the licence, defining metadata for dataset, deploying/publishing
Others	Please further explain
Notes	The HRB is currently not covering the cost of long-term preservation of data

Please note this list is not exhaustive and aims to provide examples only of eligible costs.

Who can help?

Support for developing Data Management Plans may be available at Host Institution level from the following people:

Jacintha Maron, *Cork Institute of Technology*
Aoife Geraghty, *University of Limerick*
Caleb Derven, *University of Limerick*
Aishling Hayes, *University of Limerick*
Trish Finnan, *National University of Ireland Galway*
Peter Corrigan, *National University of Ireland Galway*
Stephen Madden, *Royal College of Surgeon Ireland*
Andrew Simpson, *Royal College of Surgeon Ireland*
Brendan Palmer, *University College Cork*
Eoghan O'Carraghin, *University College Cork*
Aoife Coffey, *University College Cork*
Darren Dahly, *University College Cork*
Niamh Brennan, *Trinity College Dublin*
Darach Golden, *Trinity College Dublin*
John Donovan, *Technological University Dublin*
Yvonne Desmond, *Technological University Dublin*
Fran Callaghan, *Dublin City University*
Paul Skelton, *University College Dublin*
Jenny O'Neill, *University College Dublin*
Therese Ahern, *Cork Institute of Technology*
Fiona Morley, *Maynooth University*