Definitive Interventions and Feasibility Awards (DIFA)

2018

Guidance Notes

Key Dates & Times

Pre-proposal applications open	**1 November 2017**
Pre-proposal application closing date	**13.00 on 13 December 2017**
Outcome of pre-application stage and invitation to full application stage	**March 2018**

*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.*

Definitive Interventions and Feasibility Awards 2018

Guidance Notes

1. Introduction

The Health Research Board (HRB) *Strategy 2016 – 2020: Research. Evidence. Action.*[1] launched in January 2016 highlights three areas of focus that the HRB will engage in over the next four years. Focus Area 2 of the HRB Strategic Plan (2016-2020) 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.

The HRB are planning a review of the clinical trial landscape during 2018. In the meantime we are now inviting applications for its 2018 Definitive Interventions and Feasibility Awards (DIFA).

2. 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 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[2] conducted in preparation for a future definitive 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 intervention

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

- Fund research teams to conduct high quality definitive intervention trials 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 discoveries and knowledge into new ways of treating patients, delivering care or changing behaviour
- Support conduct of trial methodology research within the context of proposed interventions
- Improve health outcomes and health service delivery

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

[2] *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*

3. 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
- Settings of care
- eHealth
- Other studies not listed above

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 a therapy or 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. Clear progression criteria to a substantive study are required. It is not possible to apply for a feasibility study, including a pilot study, and the associated definitive intervention trial 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. These must be costed within the funding envelope provided. 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 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 AllTrials 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. Funding available

The HRB plans to commit in the region of up to €18 million over the lifetime of the strategy (2016-2020) to support healthcare intervention studies. This is the second 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 €1,000,000 (inclusive of overheads) with duration of typically 2-4 years (but not beyond 60 months).

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. The HRB acknowledges that feasibility studies for complex interventions may incur higher costs than feasibility studies for RCTs. We expect that feasibility studies for RCTs will have a significantly lower budget of below €380,000. This may be higher in exceptional cases where suitably justified.

Note: The HRB cannot take on the role of sponsor for clinical studies within the scope of the EU Clinical Trials Directive. Plans for appropriate **sponsorship** arrangements must be included in the full application i.e. Letters of Support must be provided from sponsors. **The Letters of Support must confirm 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.**

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. Research Team

Eligibility criteria

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 project. Appropriate multi and inter disciplinary involvement in the research team is essential. Where relevant, experts in trial methodology, statistics, trial management, health economics, health service research, behavioural science, qualitative research methodologies, psychology, sociology etc. should be included as Co-Applicants or as official Collaborators. 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.

Lead Applicant

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.

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

Co-Applicants

Up to a maximum of **5 research Co-Applicants** can be included. 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. 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.

Collaborators

Up to **10 Research Collaborators** can be included. 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.

Relevant key gatekeepers should be named as Collaborators within your application form if the success of a project 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. Other supports

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) 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 project (including those provided as in-kind contributions).

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.

Public and patient involvement (PPI) in research

Note: The HRB are currently planning a public review process for this scheme to provide specific feedback to applicants on the quality of their PPI plans. This feedback will be independent of the peer review process and will **not be shared with the panel**. However, panel members might take PPI approaches into consideration under any of the assessment criteria.

The HRB promotes the active involvement of members of the public in the research that we fund. This 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. PPI is research carried out '**with'** or '**by'** members of the public rather than '**to'**, '**about'** or '**for'** them. It is distinct from and additional to activities which raise awareness, share knowledge and create a dialogue with the public and it is also distinct from recruitment of patients/members of the public as participants in research.

PPI represents an active partnership between members of the public 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 project or in carrying out the research.

Involving members of the public 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 the 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
- 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.

In the application, you are asked to describe any public involvement in your research throughout the various stages of research design, conduct, analysis and dissemination. We recognise that the nature and extent of active public involvement is likely to vary depending on the context of each study.

Participation in international studies

For applications joining an international study please give details on the status, funding source, recruitment targets and outline the role of the Irish applicant as lead of the study or as participants. **Applicants 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 project feasibility.

7. Application and assessment process

Applications must be completed and submitted through the HRB online Grant E-Management System (GEMS) (https://grants.hrb.ie). GEMS will close the Pre-Application stage automatically at **1pm on 13 December 2017.**

This scheme will have a two phase application process

1. Open call for Pre-Application stage
2. Invitation of selected applicants to submit a Full Application.

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.

The HRB is committed to an open and transparent 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 in each stage of the process.

The **HRB Gender Policy** came into effect on 1 June 2016[3]. 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

Pre-application stage

The Pre-application form will focus on:

1. Case for the study
2. Potential impact of the study
3. Research team and environment

These aspects will form the assessment criteria for pre-applications, and will have equal weight.

Submitted pre-applications will be checked for eligibility. Eligible applications will be short listed by an international review panel. Members of the review panel will reflect a range of disciplines,

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

methodologies and expertise appropriate to the scheme. Feedback will be provided to all applicants after the pre-application panel meeting.

Full application – by invitation only

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 small revisions from pre-application to full application stage especially if addressing the panel feedback from the pre-application stage. Full applications should reflect a development of the relevant pre-application rather than a radically different approach.

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

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.

Stage 2 – Panel

The Full Application Panel will comprise of an independent Chair and six to eight members. It is envisaged that many 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.

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
2. Potential for impact of the study
3. Research team and environment
4. Appropriate methodology
5. Feasibility of the study

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.

8. Timeframe

Pre-Application Stage	
01 November 2017	Call opening
13 December 2017	Deadline for pre-application submissions
Jan/Feb 2018	Panel review period
March 2018	Short listing and invitations to submit full proposal

Full Application Stage	
Mid May 2018	Deadline for submission of full applications
Late August 2018	End of peer-review
September 2018	Right to reply phase
Late October 2018	Full proposal panel meeting
December 2018	Board approval
Feb/March 2019	Earliest start date of awards

9. 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

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: Detailed Guidance on the Pre-Application Form

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-Applicants.

- 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'.

Host Institution and Signatory Notification

Host Institution

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/**. Identify a Host Institution from this list and type it into GEMS in full (do not use acronyms such as UCD, TCD, NUIG). Once you have entered the first 3-4 characters of the HI, you will be assisted with auto-select options. It is important that the HI name is entered accurately and in full, as an incorrect entry may result in delays in attaining HI approvals.

If your Host Institution does not appear in this list, your Host Institution must complete the "HRB Host Institution Application Form" available on our website and return the completed form to **Hostinstitutions(at)hrb.ie. *Please note the application process for Host Institution approval is separate to the award process and your Host Institutions application may not be reviewed within the timeframe allowed for the DIFA 2018 applications.***

Signatory Notification (within Host Institution)

Once the Host Institution is selected at the initial stages of application creation this will allow the Lead Applicant to notify the authorised signatory (Dean of Research or equivalent person authorised to endorse research grant applications for the Host Institution) in that Host Institution of the Lead Applicant's intention to submit an application to the DIFA 2018. The signatory's details are pre-populated in the system so the applicant just needs to click 'NOTIFY' within GEMS. We recommend that you **notify the HI signatory** of your intention to apply as soon as possible in the application process. The signatory will receive an email from GEMS with the name and email details of the Lead Applicant and if they have any queries or clarifications they can engage directly to resolve them with the Lead Applicant. The HI signatory must confirm their willingness to participate as HI for the application through GEMS and once they do this 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.

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.

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.

Co-Applicants

The Lead Applicant can add up to 5 Co-Applicants to an application by entering 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 will inform them that they have been invited by the Lead Applicant to participate on the application as a co-applicant. 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.

Project Details

Project Title

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

Acronym

Acronym is optional.

Project Duration and Start date

Please indicate the expected length of the proposed project in months and the proposed start date. The HRB expects these awards will typically be between 24 to 48 months in duration (but no longer than 60 months). The earliest start date is February/March 2019.

Project Abstract

This should be a succinct summary of the proposed research. The aims and hypotheses of the project should be conveyed with clarity. The objectives of the project 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. Where appropriate, attempts should be made in the abstract to label the project as a definitive intervention or as a feasibility study. The word limit is **350 words**.

Keywords

Please enter up to 5 keywords that specifically describe your research project.

Study Type

Please select a study type: Definitive Intervention or Definitive Intervention & Study within a Trial (SWAT) or Feasibility study or Feasibility study & SWAT.

- *The HRB accepts that the terms 'pilot' and 'feasibility'[4] [5]are not mutually exclusive. Feasibility is an umbrella term which encompasses any study assessing the viability of a future study. The HRB defines* ***Pilot studies*** *as studies in which the future definitive study, or parts of it, including the randomisation or non-randomisation of participants, is conducted on a smaller scale (piloted) to see if it can be done. They resemble the main study in many respects including the assessment of the primary outcome.* ***Pilot studies are a subset of feasibility studies****. All pilot studies are feasibility studies but not all feasibility studies are pilot studies. A well conducted pilot study should give a clear list of aims and objectives within a formal framework which will encourage methodological rigor, ensure that the work is scientific valid and publishable and will lead to high quality trials. They are focused on the processes of the main study to ensure recruitment, randomization, treatment and follow-up assessments all run smoothly.*
- ***Feasibility Studies that are not pilot studies*** *are studies in which investigators attempt to answer a question about whether some element of the future intervention* ***can be done*** *but do not implement the intervention to be evaluated or other processes to be undertaken in a future study, though they should be addressing the future study in some way. They are not pilot studies as no part of the future study is being conducted on a smaller scale. They are used to estimate important parameters that are needed to design the main study.*

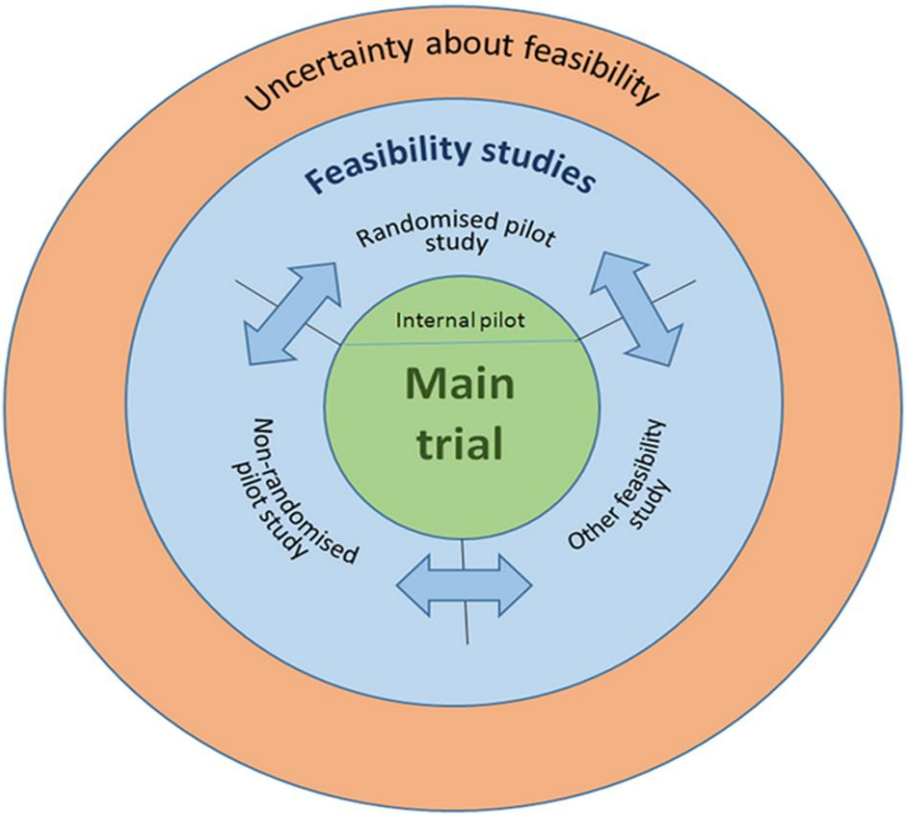

Figure 2: Conceptual Framework

[4] *Eldridge S. et al. "Defining Feasibility and Pilot Studies in Preparation for Randomised Controlled Trials: Development of a Conceptual Framework"*

[5] *Gillian A. Lancaster et al. Design and analysis of pilot studies: recommendations for good practice. Journal of Evaluation in Clinical Practice, 10, 2, 307-312*

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 project.
The Project Description should provide an overview under the following headings:

- Relevance and rationale for research
- Overall aim
- Objectives and deliverables
- Brief overview of research design and methodological approach

(Please note at full application stage applicants will be asked to include the systematically gathered evidence base for this research including a protocol to show how the search was conducted, including literature and clinical trials registries.)
The word limit is **1,000 words**.

Impact Statement

Please provide an overview of 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).
The word limit is **250 words**.

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 term 'public' 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. The HRB recognises that the nature and extent of active public involvement is likely to vary depending on the context of each study. Please provide details of where there has been public involvement in the preparation and/or design of this application. Provide details of proposed future public involvement in later stages (e.g., conduct, analysis and/or dissemination). Provide information on the individuals/groups and the ways in which they will be involved. If you feel that this is not applicable to your application you must explain why.
*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.*
Useful resources including practical examples of involving members of the public in your research can be found in Appendix III.
The word limit is **100 words**.

Project Budget

Please provide a summary and brief justification of the costs and duration associated with the project. HRB funded costs are detailed on page 30. Please refer to the HRB-CRCI checklist **https://www.hrb-crci.ie/** for guidance on trial costs. A more detailed budget will be required at full application stage.

Details of Research Team

Lead Applicant's Role

Give an outline the role of the Lead Applicant 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 a proportion of a full time equivalent (FTE).
The word limit is **100 words**.

Co-Applicant's Role

Give an outline 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 **100 words**.

Collaborator's Role

Include details of all collaborators involved in the project and state their contribution to the project.
The word limit is **50 words**.

Personnel

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

Give a brief justification for requested personnel relative to the scale and complexity of the project. *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 **100 words.**

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 **200 words.**

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) 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 where justified). An infrastructure agreement form will be required at full application stage.
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.
The word limit is **200 words.**

Submission of Pre-Applications

The deadline for submission of complete applications is 13 December 2017 at 13:00.

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 invitation to full-proposal submission

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 II: Detailed Guidance on the Full Application Form

Please note supplementary guidelines may be provided at time of full proposal invitation

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-Applicants.

- 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:***

Host Institution and Signatory Notification

The HRB strongly recommend that applicants give their Host Institution sufficient notice and time (<3 weeks) to review the application for detailed costing and approval. Please liaise with your Host Institution regarding any internal deadlines.

Host Institution

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/**

Identify a Host Institution from this list and type it into GEMS in full (do not use acronyms such as UCD, TCD, NUIG). Once you have entered the first 3-4 characters of the HI, you will be assisted with auto-select options. It is important that the HI name is entered accurately and in full, as an incorrect entry may result in delays in attaining HI approvals.

If your Host Institution does not appear in this list, your Host Institution must complete the "HRB Host Institution Application Form" available on our website and return the completed form to **Hostinstitutions(at)hrb.ie. *Please note the application process for Host Institution approval is separate to the award process and your Host Institutions application may not be reviewed within the timeframe allowed for the DIFA 2018 applications.***

Signatory Notification (within Host Institution)

Once the Host Institution is selected at the initial stages of application creation this will allow the Lead Applicant to notify the authorised signatory (Dean of Research or equivalent person authorised to endorse research grant applications for the Host Institution) in that Host Institution of the Lead Applicant's intention

to submit an application to the DIFA 2018. The signatory's details are pre-populated in the system so the applicant just needs to click 'NOTIFY' within GEMS. We recommend that you **notify the HI signatory** of your intention to apply as soon as possible in the application process. The signatory will receive an email from GEMS with the name and email details of the Lead Applicant and if they have any queries or clarifications they can engage directly to resolve them with the Lead Applicant. The HI signatory must confirm their willingness to participate as HI for the application through GEMS and once they do this 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.

Lead Applicant, Co-Applicants and Collaborators details

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.

Additional evidence of experience and expertise relevant to this application

The Lead Applicant may also wish to include any additional experience or expertise that will support their application. For example, previous experience of conducting or evaluating trials and interventions. Please state the total number of your peer reviewed publications. The word limit is **300 words**.

Co-Applicants

The Lead Applicant can add up to 5 Co-Applicants to an application by entering 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 will inform them that they have been invited by the Lead Applicant to participate on the application as a co-applicant. 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.

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) **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) under 'Manage my Details' section of GEMS and this information will be automatically included in any application that involves this individual. Please state the total number of your peer reviewed publications.

Collaborators Details

The Lead Applicant can add up to 10 collaborators per application. 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.

Project Details

Project Title

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

Acronym

Acronym is optional.

Project Duration and Start date

Please indicate the expected length of the proposed project in months and the proposed start date. The HRB expects these awards will typically be between 24 to 48 months in duration (but no longer than 60 months). The earliest start date is February 2019.

Project 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. The difference is that it needs to be written as a plain English summary such that it is clear, easy to understand, and is easily accessible to a lay audience. 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 may also be part of the feedback regarding your PPI plans. The word limit is **300 words**.

Project Abstract

This should be a succinct summary of the proposed research. The aims and hypotheses of the project should be conveyed with clarity. The objectives of the project 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. Where appropriate, attempts should be made in the abstract to label the project as a definitive intervention or as a feasibility study. The word limit is **350 words**.

Study Type

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.

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 project.

The Project Description should include:

- Relevance and rationale for Research based on systematically gathered evidence from the literature (e.g. systematic reviews or other formats of evidence synthesis)
- Overall aim
- Objectives and deliverables (including gantt chart, see template provided)
- Research design and methodological approach
- Impact statement
- Trial management, governance and safety Monitoring
- Potential risks and ethical concerns
- Compliance with data protection regulations
- Dissemination and knowledge exchange Plan

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 principle 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.
- Will the results be generalizable beyond the research setting of the study?

The word limit is **1500 words.**

Are any relevant studies listed on international registries? (i.e. European Clinical Trials Database (EudraCT, International Clincial Trials Registry Platform (ICTRP). If yes please provide study registration number(s).

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.**

Evidence from previous feasibility studies (compulsory for DI Study)

Where available, 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 finalisation of the protocol for the final definitive study.
- Provide details on the screening and recruitment rates achieved during the feasibility study.
- Provide assurances that you are confident that the intervention can be consistently implemented as intended.

The word limit is **500 words.**

If your research proposal is part of a larger international study, please provide the full protocol and 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 that how the study is progressing and any issues that may be relevant for reviewers. The role of the IDMC is outlined in Appendix V.

Overall Aim

Please state the overall aim of the research project. Explain how your proposed research is within remit of the DIFA. Include a clear explanation of the main research question phrased in PICO[6] terms where 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 **150 words.**

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. 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 estimate/summarise the 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.

Discontinuation Criteria (if applicable)

Please specify reasonable "stopping rules" or discontinuation criteria which may be applicable to your project:

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

[6] *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.*

- 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 project 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.**

Research Design and Methodological Approach

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.

Justify the **choice** of your planned intervention. Please consider following the TIDieR[7] 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. You are strongly advised to seek advice and input from an experienced research design and statistics expert at study design phase.

In addition to describing the feasibility study, you must also provide a brief description of any information relevant to the planned intention to conduct a definitive study in the future with clear progression criteria, even though it is not part of this application.

Please address the following and consider reviewing Appendix III:

- 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, conventional parallel group RCT as opposed to cluster, factorial or stepped-wedge design etc.)?
- Describe the population to be studied
- What is the planned intervention?
- Have you fully described 'usual care' (if appropriate)?
- 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?
- Identify and explain how you address gender issues in your research. Define gender differences and inequalities, for instance with respect to accessibility or utilization of health care services.

[7] *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
- What are the proposed primary and secondary outcome measures? For surrogate outcome measures, provide evidence of validity. State 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, 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 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 size of the difference is the trial powered to detect?
- 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 acceptability testing been considered?
- What is the proposed type of analyses?
- What is the proposed frequency of analyses?
- Are there any planned subgroup analyses?

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.*
- *In cases 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), the Lead Applicant must ensure that they clearly and explicitly explain any potential and/or perceived conflicts by addressing the following issues within the relevant sections of the application form:*
  - *Clarity on governance arrangements;*
  - *Clarity on roles and responsibilities;*
  - *Necessary assurances in relation to access to data, IP and publication of results/findings*
  - *Any other important issue to be highlighted by the team*
- *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.*
- *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 IV.*

Studies within a Trial (SWATs)

Are you planning to include **Studies 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. 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.

By way of examples, titles of published SWATs include:

- Site visits by the principal investigator to improve recruitment in a multicentre randomized trial.
- Timing and mode of delivery of a self-completion questionnaire.
- Gender of the person signing an invitation letter for a prospective study.
- Telephone screening versus face-to-face screening for the identification of participants in a multicentre trial.

The word limit is **500 words.**

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. If yes, provide details of feasibility studies completed and results.

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.

The word limit is **500 words.**

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 term 'public' 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. The HRB recognises that the nature and extent of active public involvement is likely to vary depending on the context of each study. Please provide details of where there has been public involvement in the preparation and/or design of this application. Provide details of proposed future public involvement in later stages (e.g., conduct, analysis and/or dissemination). Provide information on the individuals/groups and the ways in which they will be involved. If you feel that this is not applicable to your application you must explain why.

*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.*

Useful resources including practical examples of involving members of the public in your research can be found in Appendix III. The word limit is **100 words**.

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). The word limit is **500 words.**

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).

The role of these committees is to oversee the day to day management of the trial
Oversee the overall conduct and progress of the trial (including the safety data and the critical efficacy endpoints at intervals)

- Review relevant information from other sources
- Ensure adherence to protocol
- Consider interim analyses
- Advise whether to continue, modify or stop a trial and
- Provide the funding agency with information and advice.

A more detailed description of the roles of the three Committees can be found in Appendix V.

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.
- Does the team involved in data management have adequate experience of data protection issues?
- Has adequate research design methodological expertise including statistical expertise been sought and incorporated within the team?
- It will be a condition of funding to register definitive interventions in an international register such as www.clinicaltrials.gov or www.isrctn.com/
- 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 a Data Monitoring Committee (DMC)
- 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.
- Indicate costings for project management, clinical research staff, auditing, monitoring, pharmacovigilance, investigational medicinal product manufacture and release (if relevant), pharmacy services, case report form design and production, data management and statistical analysis.
-

The word limit is **2000 words.**

Participants involved in the trial

In the following sections, please list (where already known) any members of your proposed management, governance and safety committees. A more detailed description of the roles of the three Committees can be found in Appendix V. 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. **(5)**
- Trial Management Group – see Appendix V. **(10)**
- Trial Steering Committee – see Appendix V. **(5)**
- Independent Data Monitoring Committee – see Appendix V. **(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. **(10)**
- 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 of the trial protocol. **(5)**

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). Ensure that the research team has the necessary expertise to carry out the study. The word limit is **500 words.**

Data protection regulations

Please provide comments on compliance with national and/or EU Data protection regulations, if relevant, especially if the study involves transfer of data outside EU, in order to ensure an adequate level of data protection. Please explain to how you will address the requirements under the General Data Protection Regulation EU 2016/679. The word limit is **300 words.**

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. The word limit is **400 words**.

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.**

Public and Patient Involvement (PPI) in the research project

The HRB encourages the involvement of individual members of the public or patients and of public advocate groups with the aim of better research and protocol design and greater usability of both the

research project and its findings. The term 'public' includes patients, potential patients, health and social care service users, carers and people from organisations that represent service users. Please describe if the public has been actively involved in the preparation of this application, and/or will be involved throughout the various stages of research design, conduct, analysis and dissemination. If yes provide details of the individuals/groups, the ways they are involved and at which particular stage of the research project. If this is not applicable to your application, please explain why. Some resources to develop this section are available in Appendix IV. The word limit is **500 words**.

Gender issues in the research project

A key objective of the HRB is to strive for gender balance in Irish health research. We encourage a balanced participation between women and men in all research activities. Please identify and explain how you address gender issues in your research.

Indicate whether a potential gender dimension may be present or could arise in the course of your proposed research:

- If so, outline how gender analysis will be integrated in the design, implementation, evaluation, interpretation and dissemination of the results of the research proposal.
- If not, outline why it is not relevant to the research proposal.

The word limit is **500 words.**

Dissemination and Knowledge Exchange Plan

Include a clear dissemination and knowledge exchange plan to indicate how information will be disseminated during and after your research. 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 project which may be undertaken to ensure adoption beyond the term of the award. The word limit is **500words**.

Project Description Support

A file upload option is available to include an attachment to support your Project Description. A maximum of 5 figures, which can be a combination of images, 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.**

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.

Details of Research Team

Lead Applicant's Role

Give an outline the role of the Lead Applicant 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 a proportion of a full time equivalent (FTE).
The word limit is **250 words**.

Co-Applicant's Role

Give an outline 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**.

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**.

Personnel

Give full details of all personnel to be funded through this project. Note that you must give a detailed justification for the nature of the research personnel relative to the scale and complexity of the project.
State the percentage of time each person will spend on the project and describe what aspects of the proposed research they will be involved in over the lifetime of the project. If funding is requested for known personnel, please include the following details: Name, address, present position, academic qualifications, professional qualifications.

Give a justification for requested personnel relative to the scale and complexity of the project. *NOTE this scheme is not a training initiative and does* ***not fund PhDs***.
The word limit is **250 words.**

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.**

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) 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 where justified).

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. **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**.

Project Budget

Please provide a summary and justification of the costs and duration associated with the project.
The maximum total value of an award is €1,000,000 inclusive of overhead contribution. **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.

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.

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. **Applicants are advised to include annual pay increments for staff and related costs (pension contribution, employer's PRSI contribution, and overhead contribution) in the budget. Applicants are also advised to include a 1% annual contingency in salaries to cover potential future national pay agreements.** As an example, a staff member on point 1 of a given scale will go to point 2 + 1% to point 3 + 2%Please state the pay scale used and the level and point on the scale. This should be justified accordingly. For appointment of Research Fellows or Senior Research Fellows evidence of position must be provided at point of award. Please note the HRB will pay salary increments. **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 10.75% of gross salary.
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. Exceptions apply where Circular letter 6/2007 applies. 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.
2. **Running Costs**	For all costs required to carry out the research including materials and consumables, survey costs, travel for participants, transcription costs etc. 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'. The following costs are ineligible and will not be funded: animal study costs, training courses/workshops for funded research personnel, inflationary increases, cost of electronic journals. <u>Note: Please see a list of costs that fall within the overhead contribution below and which should not be listed under running costs.</u>
3. **Equipment**	Funding for suitably justified equipment can be included in this section. Personal/Stand-alone computers <u>will not</u> 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.
5. **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) 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: recruitment costs, bench fees, office space, software, contribution to gases, bacteriological media preparation fees, waste fees, bioinformatics access.

History of Application and Other Funding

History of the application (if applicable)

Please indicate whether this or a similar application has previously been submitted to the Health Research Board for review. If yes, in instances where your proposal was unsuccessful, please outline how your current proposal differs from the previous application. In instances where your previous proposal was funded, please outline how it contributed to the progression of this research. The word limit is **200 words**.

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.

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. The word limit is **500 words**.

Ethical Approval and Clinical Trial 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. Necessary authorisations for trials involving medical devices differ depending on the device. Applicants are responsible for ensuring that all necessary approvals are in place prior to the start of the research.

If any of the following documents, ethical approval and/or clinical trial approval and/or hospital approval, have already been secured for this grant you will be requested to upload a copy of the relevant approval letter later in this application.

Applicants should allow sufficient time to obtain ethical and/or competent authority approval as a copy of any of these approvals must be submitted to the HRB before the start of the award. It is suggested that these are sought in parallel with submission of an application to the HRB.

Sponsorship for Clinical Trial Applications

For applications including clinical studies that fall within the scope of the EU Clinical Trials Directive, the HRB cannot take on the role of sponsor. Plans for appropriate sponsorship arrangements must be included in the application i.e. Letters of Support must be provided from sponsors

Nomination of International Peer Reviewers

You are allowed to nominate a maximum of **two individuals that could act as peer reviewers** for your proposal in the HRB international peer-review process. The individuals nominated by you may or may not be contacted by the HRB. Please refer to HRB Conflict of Interest Policy for further details.

Submission of Applications

The deadline for submission of complete applications will be mid May 2018 at 13:00

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/

Appendix III: 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 IV: References/Useful Links

Study design

"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 (2010)
http://www.hiqa.ie/publication/guidelines-economic-evaluation-health-technologies-ireland

HIQA Guidelines for the budget Impact Analysis of Health Technologies in Ireland (2010)
http://www.hiqa.ie/publications/guidelines-budget-impact-analysis-health-technologies-ireland

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

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

Registration

International Clinical Trials Registration Platform: **http://apps.who.int/trialsearch/Default.aspx**

European Clinical Trials Database (EudraCT): **https://eudract.ema.europa.eu/results-web/**

All Trials Initiative: http://www.alltrials.net/

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
http://www.equator-network.org/resource-centre/library-of-health-research-reporting/

Clinical Research Infrastructures

Health Research Board Trials Methodology Research Network (TMRN)
http://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/#critical-care

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

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

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

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/default.aspx

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**

Clinical Research Support Centre (Northern Ireland)
http://www.crsc.n-i.nhs.uk/

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

All Ireland Hub for Trials Methodology Research
http://www.qub.ac.uk/research-centres/CentreforPublicHealth/Research/TheAll-IrelandHubforTrialsMethodologyResearch/

Public and Patient Involvement

Public Involvement Impact Assessment Framework (Provides tools to assess the impacts of involving members of the public in their research in individual projects)
http://piiaf.org.uk/

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
http://www.lindalliance.org/Patient_Clinician_Partnerships.asp

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

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

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
http://www.molecularmedicineireland.ie/page/g/t/103

NCI Best Practices for Biospecimen Resources
http://biospecimens.cancer.gov/bestpractices/2011-NCIBestPractices.pd

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

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

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

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

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

Appendix V: 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.