Clinical Trial Networks (CTN) 2021

Guidance Notes

Key Dates & Times	
Applications open	**23rd September 2020**
Application closing date	**13.00 on 1 December 2020**

Pre-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 should read the "Detailed guidance on the Pre-application Form", appended to this document prior to completing the pre-application form.

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1. Introduction

The Health Research Board (HRB) *Strategy 2016 – 2020: Research. Evidence. Action.*[1] sets out the aim to support the design, conduct and evaluation of healthcare intervention studies in order to improve health outcomes and health service delivery. Our current strategy commits the organisation to consolidate and build on progress made in constructing a coherent and integrated **clinical trials infrastructure** nationally (including facilities, coordination, research support, and networks) to deliver such interventions. The upcoming strategy 2021 – 2030 will build on the achievements made.

Since 2010, HRB has been driving the growth of clinical trials in Ireland and putting in place the supporting infrastructure. In that period the HRB has invested over €100m in clinical trials infrastructures with the overall aim of facilitating clinical trials and clinical research in Ireland that can benefit patients, the health system and the economy. HRB recognises that healthcare interventions, including trials, are an essential step in translating research discoveries into improvements in health and health services. It commits the organisation to consolidate and build on progress made in constructing a coherent and integrated clinical research infrastructure nationally (including facilities, coordination, trial support, and networks) to deliver such interventions. Intervention studies may be hospital or community based, and may include for example medicinal products, procedures, devices, behavioural treatments, preventive care or service change.

HRB Investment to date has been made in three Clinical Research Facilities (CRF) in Ireland, to provide the infrastructure (facilities, expert advice, research nursing support etc.) to conduct trials in any area of health. Individual Clinical Trial Networks (CTNs) have been funded to support communities of researchers in specific disease or health areas to develop and deliver a portfolio of trials. HRB Clinical Research Coordination Ireland (HRB-CRCI) was established as a national resource to develop Ireland as a location for clinical trials by making it easier, more efficient and faster to set up and conduct multi-centre studies. Finally, HRB-Trials Methodology Research Network (HRB-TMRN) has been funded as a national network to improve the quality of trials by driving trials methodology research on the island of Ireland, advising researchers, and engaging in education and capacity-building in trial methodology.

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

In 2020, HRB is launching a number of calls for new investment in clinical trials infrastructure. In this next phase of investment, HRB will build on national investments and adopt a co-investment model with the Health Service Executive (HSE), universities and other stakeholders to develop a world-class clinical trials infrastructure with the capacity to deliver high-quality clinical trials.

HRB is now launching a new call for **Clinical Trial Networks** which will support activities of a number of established networks in Ireland with the aim of enabling the development and delivery of a high-quality portfolio of investigator-led trials with relevance to health and social care needs in Ireland. **Awards will only provide funding for activities aimed at facilitating and developing the networking and coordination aspect**, with funding for trial activities being provided through separate, competitive sources (such as the HRB Definitive Interventions and Feasibility Awards scheme).

2. What are HRB Clinical Trials Networks?

HRB Clinical Trials Networks (CTNs) involve a formal collaboration of Researchers Health and Care Practitioner [2], patients and/or healthy people, health and care practitioners, health researchers and clinical trial staff to conduct multi-centre clinical trials (RCTs and other intervention study designs involving humans) on selected health themes across Ireland with high health, scientific, societal and economic impact.

For the purpose of this call we are seeking applications from **established clinical trial networks** in Ireland. While each Network shall be unique in some respects, HRB expects that all will:

- Have a team of applicants that brings in a spectrum of Researchers - Health and Care Practitioner, health and care practitioners, methodologists, health researchers and PPI contributors at appropriate levels of contribution and engagement
- Have a Network Lead with the time and ability to bring together relevant stakeholders and lead the development of the Network
- Within the team have a record of internationally-recognised research achievements and demonstrated ability to lead a major collaborative clinical trial at a national or international level
- Have strong links to CRF/Cs and/or other relevant infrastructural resources, and use their expertise and capability to deliver the programmatic activity as far as feasible
- Plan to conduct at least one multi-centre definitive intervention during the term of the award and to develop a pipeline of future definitive interventions
- Provide educational and training opportunities

[2] Defined as a Health and Care practitioner who is engaged either wholly or partly in clinical service provision, and actively engaged in research. They may also have an academic affiliation.

- Form effective partnerships with industry to conduct industry-sponsored clinical trials[3]
- Leverage complementary funding from other sources towards sustainability after five years. For this purpose, each network as an entity (not the individual members) should target funding in the range of €4 – 5 Million from successful applications during the term of the award. Examples of other sources of funding include European projects, other HRB funded programmes, collaborations with industry or other national or international funders
- Achieve a contribution towards Network activity costs from the overhead contribution of leveraged funding.

Minimum requirements for all applications

- Networks will be expected to demonstrate a history of team members working together to develop/deliver **registered clinical trials** over the previous four-year period. Networks may or may not have been previously funded by the HRB
- High-level strategy for the network, including the proposed portfolio and areas of particular strength
- High-level five-year business plan as part of the full proposal application to provide a roadmap for visibility and sustainability of the network
- At least 0.5FTE post for a Network Manager (or similar) must be either included in the application budget or funded through other sources. Funding must be confirmed for the duration of the new CTN award
- Publicly visible process for selection/prioritisation of studies
- Named advisory committee [4]
- A clear succession plan for the leadership of the network
- Cost-recovery model for trials and associated activities towards maintaining the network
- It must be clear that HRB investment has added value. HRB funding is not intended as a replacement for existing financial support from the Host Institution/Hospital/other funding partner
- **Networks which have previously received HRB funding under the CTN-2014 call** will be required to confirm a level of co-funding equivalent to 0.5 FTE of the Network Manager salary at time of application.

3. Aim and Objectives

[3] HRB encourages formation of strategic partnerships with industry with the ultimate aim of advancing new technologies and innovations to benefit patients. We expect that the Network will put in place appropriate policies (publicly visible) to ensure transparency, and to safeguard the independence of the research team

[4] At least one PPI Representative is expected on the Committee, and preferably two

The **overarching aim** of the HRB Clinical Trial Network awards is to enable cohesive Networks in specific thematic areas with an agreed research strategy to design, lead and conduct a portfolio of internationally competitive investigator-led, registered clinical trials.

The purpose of this call is to:

- Provide support to facilitate coordination and strategic planning for the network, support seeking funding for trial activity, and ensure shared decision-making and appropriate governance
- Fully embed PPI into the network activities from portfolio development and prioritisation to delivery of trials
- Pro-actively establish and grow international and industry partnerships, as appropriate to the portfolio
- Lead to improvements in the health and wellbeing of the Irish nation

Awards are to support *network activities only*: **funding for individual trials and interventions is not provided in this round.**

4. Scope

The scheme will provide funding for the support of existing networks that have the potential to deliver multi-site clinical trials and other interventions in Ireland. HRB investment should enable more stable operation, added-value, and additional network activity for each collaborative network, with the potential to expand the network, linking to international efforts as appropriate, and support early-career researchers to build capacity.

The scheme will provide support towards Clinical Trials Networks specifically focussed on **thematic areas of importance to patients and/or public health and wellbeing and/or health care needs**. These thematic areas will be guided by the pre-existing structures and expertise, active collaboration, research quality and high scientific added value of the proposed network as measured by international peer review. These should also align with the needs of patient populations in Ireland. **Public and Patient Involvement is expected to be a key determinant of study prioritisation within the network.**

Networks must be of a scale and scope to make an impact nationally in the specific area of research as well as being internationally competitive towards self-sustainability. They must demonstrate added value above and beyond any collaboration or networking that is currently taking place.

Out of scope for this scheme:

- **This scheme will not provide funding to establish new networks.** Networks will be expected to demonstrate a history of working together to develop/deliver **registered clinical trials** over the previous four-year period.
- **Funding for individual trials and interventions is not provided in this round**

- Given the HRB investment in Cancer Trials Ireland, **applications from networks in the area of cancer are not eligible.**
- Applications that are based on researchers from **fewer than three centres**
- Applications from individuals applying for, holding, or employed under a research grant from the tobacco industry.

5. Funding and Duration of Awards

The award will offer **network-related costs** such as salary for staff to coordinate and support the network (Network Manager[5], PPI Coordinator, Administrative support, Business Development role, Regulatory Affairs support, Trial design expertise, Data Management expertise etc), training, travel costs (including travel bursaries/international exchange visit costs), PPI costs, evidence synthesis costs, dissemination costs, outreach costs, and overhead contribution[6]. **A Network Manager/Programme Manager must form part of the network for the duration of the award as a minimum requirement**; these costs should be included in the budget if they are not funded from alternate sources. **The award cannot be used to support staff specific to a study.**

A small level of seed funding will be allowed (maximum of 10% per annum) for activities that will enhance the potential for new trials to be conducted by the network, such as providing training and exchange opportunities for early career researchers, supporting the development of patient relevant outcome measures as part of Core Outcome Sets. A process for allocation of such seed funding needs to be outlined by the team as part of the application, and this process will be subject to approval by HRB.

Funding will be up to a maximum of €1,000,000 per award, inclusive of overheads at 25%. The duration of the awards will be between 36 and 60 months; shorter durations can bid for a pro rata proportion of the maximum amount. In this round of HRB Clinical Trials Networks, **no funding will be provided for individual trials (definitive interventions or feasibility studies)**. The network is expected to source funding for future individual trials through competitive means, such as the HRB DIFA scheme.

Awards must commence in 2021. The earliest start date is Sep 2021. Awards will not extend beyond 2026; applicant teams can request funding for costs incurred from 2021 through 2026.

Co-funding from network partners is welcome either as contributions in-kind, or combinations of cash and in-kind contributions. The network should have a policy on managing contributions from industry collaborators. It must be clear that HRB investment has added value; that it enables the network activities

[5] The Network Manager would be expected to have a specific role in supporting the CTN Leads to develop/refine their research strategies or roadmaps, including management of all relevant committees, Advisory Boards etc, and managing communication with key stakeholders. Where there is no specific Business Development role, the Network Manager would be expected to also support Business Development with a focus on sustainability of the CTN

[6] This list of costs is indicative only

to be sustained over a longer period, or that it allows the network to expand the scale and scope of their activities. **HRB funding is not intended as a replacement for existing financial support from elsewhere;** this investment is intended to stimulate further investment.

It is expected that up to 6 Clinical Trials Networks will be supported in this round, quality permitting.

Funding for **Network activity** will drive a coherent network group, support PPI activity, develop a comprehensive research strategy and programme, support the writing of grant applications, and engage with potential academic and industry partners[7] as well as the relevant part of the Irish health system (e.g. HSE Clinical Care Programme). Public and Patient Involvement activities are expected to be a core part of the work of the Network. Funding may for example be used for backfilling some sessions for the Network Lead, a dedicated part role in business development or a coordinator role, training for the network or other areas as appropriate and justified.

Eligible costs include:

- ***Contributions to Personnel costs:*** *for example* costs of backfill of approximately 10% for Network Lead*, Network Manager, business development resource etc
- ***Running costs***: *for example* travel costs, meeting costs, training and exchange opportunities, networking events, access to expertise in Data Management, evidence synthesis, provision for seed funding
- ***Dissemination and knowledge exchange costs***
- ***Overhead contribution*** of 25% TDMC**

**HRB will fund up to 1 session per week of protected time for network activity work for the Network Lead only, not for Co-Applicants.*

***Total direct modified costs (excluding equipment or fees)*

6. Eligibility Criteria of the Network Applicant Group

6.1. Definitions of Network Applicant Group (Lead Applicant, Co-Applicants and Collaborators)

The *Network Applicant Group* is defined as the combined set of Lead Applicant and Co-Applicants that submit a proposal for funding under the HRB Clinical Trials Networks call. A Network Applicant Group should have as its basis a pre-existing group based on previous (multi-centre) trial work and may expand/enhance this group for the purpose of submitting a proposal to this call.

Any Network Applicant Group must encompass the necessary depth in scientific expertise, geographic cover and access to relevant patient populations required for their specific thematic area relative to the

[7] HRB encourages formation of strategic partnerships with industry with the ultimate aim of advancing new technologies and innovations to benefit patients. We expect that the Network will put in place appropriate policies (publicly visible) to ensure transparency, and to safeguard the independence of the research team

scale and scope of the proposed Network. They must also have adequate representation from patients or patient representative groups and it is encouraged that they also have knowledge users[8] as part of the team.

The HRB is deliberately not prescriptive about what constitutes such necessary depth to allow for initiatives ranging from community-based thematic areas to those relevant to a few specialist centres. There must be a core group with previous experience of delivering trials together. Please contact the HRB if you wish to check for eligibility of a specific group.

The applicant team may designate two Co-Lead Applicants for the network, at least one of whom must be a Health and Care Practitioner practising in Ireland. *They will have overall responsibility for delivery of the objectives of the Network.* The division of responsibilities between the Co-Leads should be clearly outlined within the application.

One of the Co-Lead Applicants will be the Network Lead on the proposal. The Network Lead will serve as the primary point of contact for the HRB during the review process and the duration of any subsequent contract. The Network Lead has primary fiduciary responsibility and accountability for carrying out the network activities within the funding limits awarded and in accordance with the terms and conditions of the HRB.

The number of Co-Applicants involved will depend on the scale and nature of the clinical trial network. The Co-Applicants have a well-defined, critical and substantial role in terms of assisting the Co-Lead Applicants with the leadership and management of the Network. PPI contributors are encouraged as co-applicants or collaborators as appropriate. It is anticipated that the majority of Co-Applicants will be based on the island of Ireland. However, where an researcher from outside of Ireland adds significant value they can be included as a Co-Applicant.

HRB expects that the Co-Lead Applicants and Co-Applicants will form the Executive Management Committee of the Network, with strategic and scientific oversight and administrative responsibility for performance.

The Clinical Trials Networks may also include collaborators for network activity. An official Collaborator is an individual who is committed to providing a focused contribution for a specific task. The Collaborator will serve under the direction of the Network Lead or a Co-Applicant and may receive funding through the

[8] A knowledge user is defined as one in a position of authority to influence and/or make decisions about health policy or the delivery of services and can act to ensure that the findings of the research will be translated to influence decision making and change within their (or other) organisations.
This is typically a health-system manager, policy-maker, health professional or clinician who is in a position to make significant changes to policy or practice. Knowledge user organisations may be Government departments, agencies, hospitals, local government, voluntary organisations, research charities, patient/consumer groups or other organisations involved in making decisions regarding the management, structuring and/or delivery of practice or policy in the Irish health and social care system.

award where justified. Involvement of a Collaborator should add value to the network (e.g. act in an advisory capacity); facilitate patient input or involvement; or contribute to the dissemination of the results of the research. Collaborators can be based in academic institutions, private enterprise, healthcare organisations or agencies, or come from the charity sector. If involved in genuine scientific collaboration, commercial partners may be included as official Collaborators. Commercial Collaborators will, in general, be expected to meet their own costs unless well justified.

If the on-going success of the network is dependent on access to specific groups, samples or data[9], you must elaborate on these details and include the relevant gatekeepers as Collaborators/Co-applicants within your application form. This will greatly assist the reviewers and panel members in reviewing aspects of commitment and deliverability of the proposed portfolio of studies. Sites involved in recruiting for studies within the portfolio may be represented within the list of collaborators.

An individual contributing to the research proposal, but not sufficiently involved to warrant listing as an official Collaborator, can be listed within the text of the network proposal.

The terms of any collaboration should be determined early and relevant agreements should be in place ideally by the onset of the award for successful networks, but no later than six months following the start of the award. The HRB advise that consideration must be given to issues such as relative responsibilities, governance arrangements, intellectual property rights, reporting and publishing, and access to data and samples when working up collaboration agreements.

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

6.1. Eligibility Criteria for Network Applicant Group

The Co-Lead Applicant(s) and Co-Applicants must come from a variety of different centres in Ireland. A network requires researchers from three or more centres in Ireland to be eligible to apply. The appropriate number of centres involved will depend on the thematic area and the scale and nature of the proposed Clinical Trial Network.

At least one of the **Co-Lead Applicants** must be a Health and Care Practitioner practising in Ireland. Both are expected to demonstrate **relevant experience and expertise in clinical trials and other interventions.**

[9] e.g. healthy volunteers or patients, vulnerable population groups, databases, samples, existing cohorts or longitudinal studies

This option of Co-Lead Applicants is intended to allow health and care practitioner researchers, who may not have previously held research grants in their own name, to gain experience in leading such awards. This option may also be used where the Clinical Lead holds the typical requirements of a HRB Principal Investigator but wishes to enable an additional Health and Care Practitioner, or health researcher to gain experience in leading a network of this nature. Where this is the case, and an earlier career researcher takes the Co-Lead position, there must be appropriate references to provision for mentoring within the context of the network.

The Co-Lead Applicant (**Network Lead**) 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 CTN 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.

At **least one of the Co-Lead Applicants** 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.

d) Both Co-Lead Applicants can only be named on one proposal submission as Lead Applicant.

The **Host Institution (HI)** for the HRB award is a HRB recognised host institution. It is normally that of the Lead Applicant (or one of the Lead Applicants where the Co-Lead Applicant option is being used), 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/**. The Host Institution agrees to provide support for the management of a multi-site research network, including

e.g. agreeing collaboration agreements between partner institutions, management of payments to co-applicants' institutions.

In addition, the Network Team must provide a **Letter of Support from the Hospital**[10] of the Network Lead, endorsing the Clinical Trial Network, noting recent trial activity in that site, and committing to support recruitment to (funded) studies of the network for the term of the award. Other associated Hospitals/community-based networks where patient recruitment will take place, must also provide Letters of Support.

Existing HRB-funded Clinical Trial Networks (except Cancer Trials Ireland) are eligible to apply, however funding for particular activities or posts cannot be duplicated.

Note: where an applicant fails to meet eligibility criteria, or the scientific and strategic remit of the application is outside the scope of the scheme, the application will be deemed ineligible and will not be accepted for review. The HRB will contact the Host Institution and Lead Applicant in the event that this situation arises.

7. Coordination with other trial infrastructures

As we enter a new phase of investment in national clinical trials infrastructure, it is critical that coordination and synergies are enhanced across the system to maximise the value of this investment.
To this end, successful awardees will be expected to **work with other clinical trial infrastructures** within the national system to collectively improve patient access to clinical trials, and to enhance supports for investigator-led trials in Ireland.

Applicants are expected to demonstrate how they will coordinate activities and maximise synergies with other trial infrastructures, for the purpose of delivering a portfolio of studies. The approach to coordination with existing research infrastructures such as the Clinical Research Facility/Centre (CRF/C), The National Clinical Trials Coordination Programme, the HRB Trials Methodology Research Network (HRB TMRN) must be described.

International coordination
Applicants should describe how they work with and are coordinated with other relevant international structures (as relevant to their portfolio), such as other International trial networks, Cooperative groups and ECRIN.

[10] Individual Hospital, Hospital group, or community/practice network where patient recruitment will occur

A Letter of Support/Infrastructure Agreement Form from all relevant clinical research infrastructures will need to be provided at time of application, clarifying how they will work with the CTN for the term of the award.

8. Public and patient involvement (PPI) in research

In line with the move to integrate PPI into HRB decision-making, HRB are currently planning a ***public review for a number of HRB calls launching in 2020 including the HRB CTN 2021****. These reviews will run in parallel with the international panel review. Comments from public reviewers will be provided to the applicants, and they will have the opportunity to respond to the public reviewer comments as part of the Applicant Response stage of review. Panel reviewers will have sight of both the public review as well as the applicant team's response, to inform their review.*

The HRB is using the definition of PPI proposed by INVOLVE: Research carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them. The HRB promotes the active involvement of members of the public in the research that we fund[11]. Public involvement 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.

'Public involvement' 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.

PPI contributors should be actively involved and part of decision making. Involving members of the public in research can improve quality and relevance of research. 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.

[11] http://www.hrb.ie/funding/funding-schemes/public-and-patient-involvement-in-research/

In addition to improving relevance and quality of research, it ensures that research is influenced by broader principles of citizenship, accountability and transparency. PPI is an ethos as well as a practice. It should be context-specific and should aim to ensure that all voices are heard. Where members of the public or patients are involved, they must be compensated for their time and contributions.

In the application, you are asked to describe any public involvement in your proposed Network. We recognise that the nature and extent of active public involvement is likely to vary depending on the context of each award. **PPI contributors should be named as Co-applicants where justified by their level of involvement.** The HRB will aim to provide specific feedback to applicants on the quality of their PPI plans through a public review process. The HRB will share the public review feedback with the PPI Ignite team in the host institution where applicable.

Applicants are asked to describe how the CTN will support and integrate PPI activities during the development of an application and throughout the award.

PPI should play a critical role in the clinical trial networks. If there is currently little or no PPI within your network this is an opportunity to attract PPI contributors to the team with a view to making the research portfolio more relevant to patients.

We strongly advise that you consult with your Host Institution who may be able to provide guidance and support on PPI in the context of the network activities.

The HRB together with the Irish Research Council are currently inviting an application for a National PPI Network, with sites across Ireland. Coordination of activities between any National PPI Network and individual CTNs is expected.

9. Network Structure: Management and Governance

HRB Clinical Trials Networks will coordinate and facilitate the Network and ensure shared decision-making and good governance. This includes strategic planning, and the driving of trial activity (led from within the Network or with academic or commercial partners) on the path to self-sustainability. This will be a key aspect of the network and will incorporate the definition or updating of a research strategy for the group, as well as a structured approach to engaging with potential partners. It is recommended that each network engages with its relevant HSE Clinical Care Programme[12] and other appropriate groups such as policy-making groups to explore synergies and facilitate the translation of research findings into practice to maximise the impact on health.

[12] http://www.hse.ie/eng/about/Who/clinical/natclinprog/

HRB Clinical Trials Networks will be expected to put an appropriate management structure in place to ensure the efficient operation of the Network. A **Management Committee** with strategic and scientific oversight and administrative responsibility for the performance of the network should be set up, including the Network Lead and the team of co-applicants as well as PPI representation. Knowledge user representation would be welcome.

Each Clinical Trials Network will also put in place additional independent governance arrangements for the Network, such as a Stakeholder Advisory Board.

In addition, individual trials undertaken by the Network will have their own governance arrangements.

10. Application and assessment process

The HRB is committed to an open and transparent process underpinned by quality, excellence and international peer review. Applications must be completed and submitted through the HRB online Grant E-Management System (GEMS) (https://grants.hrb.ie). GEMS will close automatically at **1pm on** Tuesday 1 Dec **2020.**

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

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

The **HRB Gender Policy** came into effect on 1 June 2016[13]. In line with international best practice the HRB has a responsibility to support both women and men to realise their full potential in order to ensure equality of opportunity and to maximise the quantity and the quality of research. To ensure fairness and equality to all applicants, each funding application received will be assessed as outlined in the call guidance documentation for that particular funding round.

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

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

ranking factors to prioritise proposals with the same scores in the Panel ranking list. As part of this application, applicants are asked to describe whether gender balance been taken into account in the at decision-making levels in the network.

Applicants to CTN 2021 will be asked to provide a high-level description of any potential **gender and/or sex differences** that may arise for their portfolio, which will be accounted for during design, conduct, analysis and dissemination of the research.

10.1 Application Process

Submitted applications will first be checked for eligibility by HRB staff against the minimum requirements for this scheme: application is in scope, both eligibility of the team, as well as minimum requirements expected of the network as a whole.
Eligible applications will undergo a Panel assessment process as follow:

Panel

The Panel will comprise of an independent Chair and five to ten members. It is envisaged that some will have served on previous HRB Panels. Panel members are selected based on the range of applications received and the expertise and skillset required.

Panel members will be assigned to review each eligible Clinical Trial Network application and provide written feedback, in addition to an initial score according to the agreed assessment criteria. Depending on the volume of applications received **this initial score may be used to shortlist applicant teams for interview.**

Applications to CTN 2021 will in parallel undergo a public review. Two public reviewers will be invited by the HRB to review each application. Public reviewers will assess the quality of PPI in the proposal and they will provide comments and a rating, but not a score. Comments from public reviewers will be provided to the applicants, and **short-listed applicants** will have the opportunity to review the public reviewer comments prior to the interview stage (applicant response stage). While **PPI** is not a stand-alone scoring criterion in CTN 2021, the international Panel reviewers will have sight of the public reviews throughout the process, and will take the written comments, rating and applicant response to the public review into consideration when reaching a consensus on each proposal.

Interview

Lead Applicants and key team members short-listed through this process will be invited to attend an interview. Initial comments or questions from the international Panel and public reviewers will be provided to the Lead Applicants prior to the interview. This will provide the Lead Applicants and their team with an opportunity to address the key comments, suggestions, misconceptions, etc. within the Panel reviews and the public reviews in a written applicant response.

The names of the panel members will be provided to the candidates a few days before the interview meeting. It will be confirmed closer to the time whether the interviews will take place virtually, or in-person at the HRB Offices, guided by any Covid-19 travel restrictions.

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

The **Criteria for Assessment** of the applications are:

- **Network relevance for health and social care needs in Ireland**
    - Important research area
    - Potential impact of Network activities (including the targeted portfolio of trials) on patients and/or public health and wellbeing and/or health care
    - Vision, scope, objectives of network clear and appropriate

- **Strength of collaboration**
    - Clear collaborative approach to decision making, strategy, portfolio development
    - Appropriate stakeholders involved
    - Appropriate Network management and governance

- **Quality of proposed network and trials activities**
    - Appropriate activities to achieve the Network vision
    - Proposed trial portfolio appropriate
    - Activities will build further capacity for future trials

- **Team and environment**
    - Expertise and track record of team in high quality relevant clinical trials
    - Appropriate skill mix
    - Accessibility and suitability of facilities, infrastructure and other supports

Each assessment criterion is weighted equally.

Public reviewers will only assess the quality of PPI in the proposal, they will provide comments and a rating but not a score.
Public Reviewers are asked to comment on the following:

- The Plain English Summary (Lay Summary)
- Relevance of the Proposed Network Theme to health and social care needs
- Public and Patient Involvement throughout the network
- Dissemination and Potential Impact of the Proposed Work.

It must be clear that HRB investment has added value; that it enables the network activities to be sustained over a longer period, or that it allows the network to expand the scale and scope of their activities. Proposals which do not demonstrate this will not be considered for funding.

The recommendations of the 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.

The HRB reserves the right to modify the review process. Applicants will be notified of any relevant modification to the review procedure.

Conflict of Interest

Conflict of interest rules *are applied rigorously*. Where a conflict of interest exists, the reviewer is requested to inform the HRB immediately so that an alternative reviewer may be appointed. International panel reviewers will not provide comments or scores on any application on which they have a conflict of interest.

Reviewers must adhere to high standards of integrity during the panel review process. They must respect the intellectual property of applicants and may not appropriate and use as their own, or disclose to any third party, ideas, concepts or data contained in the applications they review.

11. HRB Oversight and monitoring

11.1 HRB Expert Advisory Group

For independent oversight and strategic leadership, the HRB will appoint a **Clinical Trials Infrastructure Expert Advisory Group** to oversee our investments in Clinical Trials Infrastructure from 2021 onwards.
The Expert Advisory Group will be established to help guide the HRB and the clinical trials community to:

- work towards **integrating clinical trials within the health system** to ensure that they are delivered as part of usual care,
- raise the **standards of the clinical trials environment and their conduct** in Ireland whilst,
- safeguarding the HRB's investment of approximately €60 million in Clinical Trials Infrastructure over the next five years.

The Expert Advisory Group will work with the HRB to review performance of all clinical trials infrastructures on an ongoing basis and will be instrumental in implementing corrective action where needed.

11.2 Award monitoring

Mandatory reporting of metrics will be required of all HRB-funded CTNs. The performance of each Network will be driven by key performance indicators (KPIs) covering both Network activity and portfolio activity. KPIs for successful applications will be agreed with the HRB prior to acceptance of the award contract. Over the lifetime of the award the success of the Network will be judged against these KPIs and the continuation of HRB funding will be dependent on reaching these KPIs.

Furthermore, awardees will be expected to report activity in relation to work with other clinical trial infrastructures, including HRB-TMRN, HRB-funded Clinical Research Facilities/Centres, The National Clinical Trials Coordination Programme, and the National PPI Network, as appropriate.

An internal review against agreed KPIs will take place at approximately 18 months to monitor progress on Network activity (as funded by the award). A scientific and strategic progress review will be undertaken by an international Panel of experts at approximately 36 months.

12. Trial Registration and Reporting

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, as well as trials delivered by networks 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.

Therefore, and aligned to the HRB Clinical Trials and Interventions Research Governance Policy[14], we will require **all interventions carried out by HRB-funded CTNs are to be registered in a publicly accessible register prior to initiation of the study, as part of their contractual obligations.** 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. These results must be posted to the results section of the clinical trial registry where the trial was originally registered.

13. GDPR

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

[14] https://www.hrb.ie/fileadmin/1._Non-plugin_related_files/RSF_files/Policies_and_principles/Grant_Policies/HRB_Policy_on_Clinical_Trials_and_Interventions_Governance.pdf

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

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

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

14. Timeline

23 September 2020	Applications for CTN 2021 open
1 December 2020	Deadline for submission of full applications
Dec 2020/Jan 2021	Application review process
From week beginning 1 Feb, dates TBC	Applicant response phase for short-listed applicants
24-26 February 2021	Interview panel meeting
Late March	HRB Board approval
September 2021	Earliest start date of awards

The deadline for submission of applications through GEMS is Tuesday 1 December by 13.00 pm.

15. Contacts

For further information on the Clinical Trials Networks contact:

Dr Karen Crowley
Project Officer
Health Research Board
e kcrowley@hrb.ie

Dr Caitriona Creely
Programme Manager
Health Research Board

Please note that the HRB will not follow up any requested supporting documentation related to the application, such as Host Institution's Letters of Support, 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/funding/funding-schemes/before-you-apply/relevant-policies/

Appendix I: Detailed Guidance on the 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. **For applications utilising the option of two Co-Lead Applicants, one Lead applicant must take on the role of submission to GEMs; their CV and contact details will be pulled through from GEMs. The second Co-Lead Applicant must enter their details manually. Both Co-Lead Applicants must review and approve the application prior to submission.**

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

Once logged in to GEMS applicants are taken directly to the Home page which is the starting point to create a new Grant application. Please select the Clinical Trial Networks (CTN) 2020.-***Further details for completing each of the main sections of application form is provided below:***

Declaration of Interests

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

Host Institution and Signatory Notification

The HRB expects that applicants contact their Host Institution as soon as they begin their application, and engage with them to facilitate a review of the application. 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. 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.

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 CTN 2021. 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.

1. Clinical Trial Network Summary

1.1 Clinical Trial Network Title

This should be descriptive and concise and should reflect the aim of the network.

1.2 & 1.3 Award Duration and Start Date

Please indicate the expected length of the award in months (minimum duration is 36 months and the maximum duration is 60 months) and the anticipated start date. The earliest start date for awards is September 2021. **Awards must start during 2021 and must complete end 2026.**

1.4 Proposal Abstract

This should be a succinct summary of the proposed CTN network activities. The aims of the CTN should be conveyed with clarity. The objectives of the CTN 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. The word limit is **500 words**.

1.5 Lay summary

This lay summary is similar to the proposal abstract in that you are asked to describe what you propose to do, say why you think it is important to complete this work, and how it will be done. 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 published on the HRB website. The word limit is **300 words**.

1.6 History of the CTN

Please provide a brief history of the CTN since its establishment. Describe the CTN in the context of the Irish health research ecosystem. Please describe how the CTN has enabled delivery of a portfolio of clinical trials.

Please summarise supports from the Host Institution/ Hospital/Associated charity or Foundation since the establishment of the network such as e.g. funding for specialised equipment, support for financial reporting, HR etc. Please give an overview of salary supports and other direct financial supports provided from the Hospital and Host Institution, and indicate duration of the support.

Please describe what is working well at present, current challenges, and what will change over the term of investment should this application be successful.
The word limit is **400 words**.

2. Lead Applicant, Co-Applicants and Collaborators details

2.1 Lead Applicant

Details are requested about the Lead Applicant, including their position, employment status (contract or permanent), whether they are seeking salary-related costs, and their experience.
The Lead Applicant's **contact and CV details** (Name, contact information, institution, present position, profession) are managed in the 'manage my details' section of GEMS and are automatically included in any application created involving that individual.

2.1.2 Lead Applicant(s) Publications and Funding Record

Lead and co-lead applicants are asked to add their **5 most relevant publications to this application** on which they have acted as senior author. Please use the publication selection tool in this section to select the 5 most relevant publications. Please note your full list of publications will not be pulled through from your CV. Please state the total number of your peer reviewed publications.
You should also include your **5 most relevant funding** awards as Lead Applicant or co-applicant.

2.1.3 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. Please describe any experience with successfully leading a network. For example, evidence of expertise they may have relating to collaborative clinical trials, commercialisation, industry involvement, PPI activities, and influencing healthcare practise and/or policy. The word limit is **300 words**.

2.2 Co-Lead Applicant (if applicable)

Please note, this option is only available where at least one of the Co-Leads is a Health and Care Practitioner researcher practising in Ireland. Details are requested about the Co-Lead Applicant and must be entered in 'manage my details' including their name, contact information, institution, present position, profession.

The Co-Lead applicant will address the same questions as the Lead Applicant (above).

2.3 Co-Applicants

Co-Applicants have a well-defined, critical and substantial role in terms of assisting the Lead Applicant with the leadership and management of the proposed Network. Co-Applicants are generally expected to lead on one or more of the proposed Network activities. **It is expected that many CTN applications will have a PPI Contributor/Lead as co-applicant.** The Lead Applicant can add up to 10 Co-Applicants to an application by entering their name on GEMS (up to a maximum of 20 co-applicants and collaborators in total).

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. PPI Participants can register in the same way as Co-Applicants.

2.3.1 Co-Applicants Contact and CV Details

Co-Applicant Contact and CV Details

Each co-applicant should ensure the following **contact and CV details** in the 'manage my details' section of GEMS are up to date and correct (Name, Contact information, Institution)

This information will be automatically included in this application. Each co-applicant must then list the **5 most relevant publications** to this application on which they have acted as senior author (first, last or corresponding or in those fields where alphabetic order authorship is the norm, joint author)**. Please note Co-Applicants 5 most relevant publications must be entered directly onto the application form and will not be pulled through from their CV.**

Co-Applicants are also asked to provide any additional evidence of expertise they may have relating to collaborative clinical trials, network membership, commercialisation, industry involvement and effect on healthcare practise and/or policy. The word limit for this is **200 words**.
Please state the total number of your peer reviewed publications.

Letters of Support: **Host Institution**

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 CTN 2021 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.

2.4 Collaborators Details

The Lead Applicant can add collaborators per application (up to a maximum of 20 co-applicants and collaborators in total). Unlike co-applicants, the information for collaborators is not automatically drawn from the 'Manage my Details' section of GEMS but must be entered by the Lead Applicant. The Lead Applicant must enter **contact and CV details** for all collaborators including name, contact information, institution, present position, **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.

3. Network Team Details

3.1 Network Applicant Group

3.1.1 Lead Applicant Role (Network Lead)

Firstly please indicate the **current commitment** to research/clinical/teaching/other, either as a percentage or a proportion of a full time equivalent (FTE). Outline the role of the Lead Applicant in the CTN on a day-to-day basis including amount of time to be spent working on the network either as a percentage or proportion of a full time equivalent (FTE). Where the Network Lead is taking on a mentoring role for the Co-Lead this should be referenced in the Role description. These descriptions should clarify the difference in roles between the two Co-Leads. The word limit is **200 words**.

3.1.2 Co-Lead Applicant Role (if using)

Please indicate the **current commitment** to research/clinical/teaching/other, either as a percentage or a proportion of a full time equivalent (FTE). Outline the role of the Co-Lead Applicant in the CTN on a day-to-day basis including amount of time to be spent working on the project either as a percentage or proportion of a full time equivalent (FTE). These descriptions should clarify the difference in roles between the two Co-Leads. The word limit is **200 words**.

3.1.3 Co-Applicant's Role[15]

Outline the role of all Co-Applicants in the CTN project on a day-to-day basis including amount of time to be spent working on the project either as a percentage or proportion of a full time equivalent (FTE). The word limit is **75 words per Co-Applicant**.

3.1.4 Collaborator's Role

Include details of all collaborators involved in the CTN and state their contribution to the project and the amount of time to be spent working on the project either as a percentage or proportion of a full time equivalent (FTE). The word limit is **75 words per Collaborator**.

3.1.5 Personnel

Complete the table with details of all personnel expected to be employed to work on this CTN. Specify the personnel type, state the time each person will spend on the project, either as a percentage or proportion of a full time equivalent (FTE), indicate which work packages(s) they will be involved in, describe their role in the proposed CTN over the lifetime of the network. If known you are asked to provide their name, present position and qualifications. A Network Manager is considered a key role within each CTN. At least 0.5 FTE **Network/Programme Manager**[16] must be provided for the duration of the award (funded by HRB or in-kind). **Please clarify whether you are requesting funding from HRB for each position.** The word limit is **75 words per person**.

Give a justification for requested personnel relative to the scale and complexity of the project.

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[15] Please note: research infrastructures are not expected to be listed as co-applicants in applications. Details should be included in Infrastructure Agreement Forms as detailed in Section 3.3

[16] The Network Manager would be expected to have a specific role in supporting the CTN Leads to develop/refine their research strategies or roadmaps, including management of all relevant committees, Advisory Boards etc, and managing communication with key stakeholders. Where there is no specific Business Development role, the Network Manager would be expected to also support Business Development with a focus on sustainability of the CTN

NB: Please note ***no PhDs or Masters will be*** *funded through this scheme; the HRB supports structured education programmes through other mechanisms including The Structured Population Health and Health Services Research Education (SPHERE), the Wellcome-HRB Irish Clinical Academic Training Programme (ICAT) and the Collaborative Doctoral Awards (CDA) scheme.* However applicants to HRB CTN 2021 may make provision for hosting PhD/Masters students on short **placements** to provide experiential learning opportunities on different aspects of trials.

3.1.6 Network Clinical Lead Profession and Occupational Speciality Environment

Please state the Clinical Leads' profession and occupational speciality, the approximate number of individuals trained in this speciality in Ireland and approximately how many of these are engaged in research and where are the main centres that this research is currently being undertaken? The word limit is **200 words**.

3.2 Strength and Complementarity of the Applicant Group

You are asked to describe how the formation of this applicant group strengthens this proposal in terms of complementarity of scientific expertise, synergistic potential and the added value of the collaboration. Show how the team has the collective expertise, competencies and experience to successfully deliver this network, under the leadership of the Co-Lead Applicant(s).

Please set out clearly **what changes to the team are proposed** for the term of the award. Does the applicant group have appropriate statistical and methodological expertise to enable them to develop a portfolio of suitably designed studies (if not then describe how this will be accessed in the next section "infrastructure and support"). The word limit is **800 words**.

3.3 Infrastructure and Support

Please detail arrangements with local hospitals and local/regional/national infrastructures regarding access to expertise, facilities or space in order to successfully deliver the CTN portfolio.

Applicants are expected to demonstrate how they will coordinate activities and maximise synergies with other trial infrastructures, for the purpose of delivering a portfolio of studies.

Please describe the approach to coordination with existing research infrastructures such as the Clinical Research Facility/Centre (CRF/C)s, The National Clinical Trials Coordination Programme, the HRB Trials Methodology Research Network (HRB TMRN[17]), Centre for Applied Medical Imaging (CAMI), other relevant Clinical Trial Networks, and the National PPI Network for the purposes of delivering the CTN activities. Applicants should describe any planned engagement in National Clinical Trials Coordination Programme Working Groups, relevant to the activities of the CTN.

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

An **Infrastructure Agreement Form** must be completed for each centre and can be downloaded from GEMS. The Form must be completed, signed, dated and uploaded on GEMS. Electronic signatures are acceptable for letters/forms that are uploaded on GEMS. Please note: research infrastructures are not expected to be listed as co-applicants in applications.

The word limit is **600 words.**

3.4 Letters of Support: Hospital/Hospital Group/community/practice network

The Network Team must provide:

(i) a **Letter of Support from the Hospital**[18] **of the Network Lead**, endorsing the Clinical Trial Network application, noting recent trial activity in that site, and committing to support recruitment to (funded) studies of the network for the term of the award, and

(ii) a **Letter of Support from each associated Hospital/community-based network** where patient recruitment will take place.

The formal letters on headed notepaper, dated and signed by the Head of the (Hospital) must include the following information; [*Hospital/Community-based network/practice network – insert name*] (i) is supportive of the application [title of application – insert name] led by investigator(s) [(Co-Lead) applicant(s) – insert name(s)], (ii) has previously supported the following trials with [name of local investigator], [name of trial], which recruited at [*Hospital – insert name*] (where appropriate), and (iii) will support recruitment to funded studies of the network for the term of the award.

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.

4. CTN Description

4.1 Rationale for the CTN

(i) Describe the background to the CTN including what is already in place, setting this clearly within a national context. Explain the rationale behind the establishment of the CTN, and the health or social care needs this is intended to address, with the size and nature of the problem in Ireland clearly communicated.
(ii) Articulate the added-value from this CTN above and beyond what could be achieved through individual awards. What would this HRB award enable that would not happen otherwise?
The word limit is **800 words.**

[18] Individual Hospital, Hospital group, or community/practice network where patient recruitment will occur

*A file upload option is available to include an attachment to support your CTN Description. This **single document** must be uploaded on HRB GEMS. This may be images, graphs, tables as appropriate. In the same document you may also upload an organisational chart and any letters of support (other than collaborators). Figures must not be embedded within the text of the Project Description. The maximum file size is **10MB.***

4.2 Overarching Strategy of the CTN

Briefly describe the strategic position of the CTN. Detail key opportunities and strategic challenges for the CTN. Please state the vision and mission of the CTN, that includes the investment term (approximate 5-year horizon expected). Please describe strategic objectives aligned with the vision and mission, to include the proposed term of HRB investment. Objectives should be SMART (specific, measurable, achievable, realistic and time-bound) and should reflect the CTN'S overarching strategy.
The word limit is **400 words**.

4.3 Impact statement

The statement should be as specific as possible and provide information that reviewers will find helpful in assessing the potential impact of this five year HRB award for the CTN. Describe expected outputs, outcomes and longer-term impacts from this investment in areas such as driving the number of quality of clinical trials in the Irish health system, training for early career researchers in trials, delivering health innovations, effecting change in health policy and practice, increasing capacity for world-class clinical trials, knowledge generation, economic development and commercial activity in a local/national/international context. The potential for uptake of the proposed research portfolio within the Irish healthcare system and its impact on practice and/or policy and decision-making should be discussed. An implementation plan that outlines the pathway to impact, citing realistic timelines is requested.

Please ensure you fully describe the role of the knowledge users in Ireland (or globally), such that reviewers can make an assessment of the potential impact of the work. Where impact is mainly anticipated in an Irish context, please describe this for international Panel members.

The word limit is **800 words**.

4.4 Core outcome sets

Please give information about Core Outcome Sets[19] that are available for your current and planned portfolio. Do these include Patient-Reported Outcome Measures[20] (PROMs)? Have patients/patient

[19] The HRB encourages the development and application of agreed standardised sets of outcomes, known as 'core outcome sets' (COS), such as those reported by the COMET (Core Outcome Measures in Effectiveness Trials) Initiative. Where COS do not exist for future studies in the portfolio, this is an opportunity to undertake development work, with patients and health care professionals as appropriate

[20] Patient-reported outcome measures are used to assess health outcomes from a patient perspective, required in some cases by regulators to support medical product labelling, and ideally patients should have direct involvement in their development: B Weiring et al Health Expect. 2017 Feb; 20(1): 11–23.

representatives/carers been involved in their development[21]? Is any work intended during the course of this award on developing/refining outcome measures to better reflect patient priorities?
The word limit is **300 words**.

4.5 Network Activities

Summarise the planned network activities for the CTN. Network activities may include but are not limited to how the network will communicate, developing PPI activities within the portfolio, supporting development of Core Outcome Sets, promoting the network, applying for additional funding to sustain the network, evidence synthesis for future studies, research prioritisation workshops, mobilising seed funding,.
Explain how the CTN leadership will manage growth and expansion of the network to engage a broader community of researchers/clinicians. Specifically explain how new members will be incorporated during the lifetime of the award and at what point will this happen. Describe education or training opportunities planned to build and develop workforce capabilities for future trials, at all levels of the team. Outline any activities targeted at earlier-career researchers.
The word limit is **1200 words.**

4.6 Trials Portfolio

4.6.1 Recent registered clinical trials

As an eligibility criterion of the call applicants will be expected to demonstrate a history of team members working together to develop/deliver registered clinical trials over the previous four-year period. Not all members are expected to have worked on each trial.

For each study Active or Completed during 2017/18/19/20[22] the following details must be given in the Excel template provided:

- Title of this study
- Registration number (only registered trials are captured here)
- Sponsor
- Principal Investigator
- Who is participating from the Network Applicant Team (please name PI, and site investigators as well as other team members such as statisticians/methodologists…..)
- Has the trial concluded?
- Did sites within Ireland recruit?
- Was planned recruitment achieved: globally?
- Was planned recruitment achieved: at the sites in Ireland?

[21] An explanatory video for patient involvement in core outcome sets (COS) can be found here: http://www.comet-initiative.org/Patients

[22] Due to the later submission date of January 2021 for this call, we are asking for registered clinical trial data up to 31 December 2020 to give a better picture of recent activity. We recognise that the data for this year may appear as an outlier due to the impact of Covid-19, however the HRB and the Panel will recognise this

- Please provide a link to reported trial outputs.

A full explanation of terms is given in the "Reference and guidelines for CTN Trial Data" document, available for download from GEMs.

Please note that only registered trials can be captured in the spreadsheet. *If there are multiple registration numbers, please quote the ClinicalTrials.gov registration number.*

4.7 Current portfolio

Please give a high-level description of the research portfolio (details of which you have provided in the Excel of on-going and recently-completed studies (2017/18/19/20)[23], demonstrating that Network Team members have worked together on registered clinical trials.

What metrics do you use to measure performance of individual trials, and of the portfolio overall? What tools/software packages do you use to aid performance monitoring?

4.7.1 Please **upload** your policy on selection and prioritisation of studies (**mandatory**)
4.7.2 Please **upload** your policy on the procedure and criteria for stopping trials, if one is available.

The word limit is **800 words.**

4.8 Planned studies

Please briefly outline planned studies for the term of the award (with proposed team members), which demonstrates the scientific breadth and depth of the network. Be aware that the peer reviewers reading your proposal will be based outside of Ireland, so it is important to describe the current healthcare delivery context in Ireland when discussing issues around need, relevance, timeliness and feasibility. Please note where sex and or gender differences will need to be considered in each case. For each proposed study, please indicate where funding has already been secured for planned studies, or if it is intended to bid for competitive funding (this should align with details in the Clinical Trial Network Sustainability section).
Explain how this work synergises with the network activities described in this application to deliver the broader research strategy.
The word limit is **1000 words.**

4.9 Seed funding

Do you intend to use part of the HRB budget as Seed Funding (Y/N)?

[23] Details of individual studies in the specified four-year period, for purpose of establishing eligibility of network, will be entered in a separate section. Due to the later submission date of this call, we are asking for registered clinical trial data up to 31 December 2020 to give a better picture of recent activity. We recognise that the data for this year may appear as an outlier due to the impact of Covid-19, however the HRB and the Panel will recognise this

If Yes, please provide a description of how you intend to use this, how much you intend to make available, and the mechanism for decision-making on allocation of funding.
The word limit is **600 words.**

4.10 Public and Patient Involvement (PPI) in the CTN

PPI should play a critical role in the clinical trial networks. If there is currently little or no PPI within your network this is an opportunity to attract PPI contributors to the team with a view to making the research more relevant to patients. Also, any activities to be coordinated with National PPI Activities should be described here.

Please **describe** all public and patient involvement at each stage in the development of and throughout the network, such as, but not limited to:

- development and prioritisation of the portfolio[24]
- contribution to work on Patient Reported Outcome Measures
- oversight
- dissemination, including End of Study information for participants.

For each stage please include the purpose of this involvement and where applicable how PPI has influenced/changed what work has been planned.
This section should be a succinct summary of public involvement activities. Provide information on the individuals/groups and the ways in which they will be involved. **Where members of the public/patients are involved, they should be compensated for their time and contributions; this should be reflected in the project budget.**
Please ensure to provide more detail in other sections as appropriate.

Important: This section 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.

*Please note PPI does **not** include the recruitment of study participants. Whilst this falls under patient-oriented research, it is participation of the public rather than involvement. It also does **not** include work aimed at raising awareness of the public around research, such as media publications of research findings, and outreach activities such as open days in research facilities.*

A number of useful links are included in Appendix IV. The word limit is **600 words**.

4.11 FAIR data management and stewardship

The HRB Policy on Research Data Management governs data gathered and generated in whole or in part from HRB-funded research from 1st of January 2020. [25] While individual Research Data Management Plans will have to be developed on a study-by-study basis, Lead Applicants should consider how studies within the CTN portfolio can ensure they are in line with policy requirements (of HRB and other funders). Please describe how you will work with support of data stewards or other data-related services support

[24] Public and Patient Involvement is expected to be a key determinant of study prioritisation within the network.
[25] https://www.hrb.ie/fileadmin/user_upload/HRB_Policy_on_sharing_of_research_data.pdf

in the Host Institution (typically library and ICT and digital services, etc) on approaches to data management and stewardship for the CTN as a whole. Please consider the FAIR Guiding Principles for scientific data management and stewardship: Findability, Accessibility, Interoperability, and Reusability[26].
The word limit is **600 words**

4.12 Dissemination and Knowledge Exchange Plan

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

Include a clear dissemination and knowledge exchange plan to indicate how the outputs from the portfolio will be disseminated and shared and made openly accessible, in line with HRB Open Access Policy[27]. Outputs may include research articles, Core Outcome Sets/PROMs, research data, datasets, clinical guidelines, educational resources, reports, policy briefs and other relevant documents. The plan should include dissemination of results to study participants. Protection of Intellectual Property should be considered before data are disseminated[28].

Who are the various audiences and communities that need to be targeted if these results are to have any impact? Describe how the findings of this research will be publicised to the HSE or wider health community in a manner that will optimise impact on health policy and/or practice. If possible, reference should be made to any aspects of the study which may be undertaken to increase likelihood of adoption beyond the term of the award.

Please note the HRB has a mandatory Open Access publication policy; demonstrate how you plan to make all publications open access.
HRB Open Research: rapid open-peer reviewed and open access platform for all research outputs, with all publication charges covered centrally by the HRB at no expense to the grantee.
(www.hrbopenresearch.org)

The word limit is **600 words**.

4.13 References

[26] Wilkinson, M. D. *et al.* The FAIR Guiding Principles for scientific data management and stewardship. *Sci. Data* 3:160018 doi: 10.1038/sdata.2016.18 (2016).
[27] http://www.hrb.ie/research-strategy-funding/policies-and-guidelines/policies/open-access/
[28] All HRB Host Institutions must subscribe to the National Intellectual Property Protocol, '**Inspiring Partnership- the national IP Protocol 2016: Policies and resources to help industry make good use of public research in Ireland**', prepared by Government/Knowledge Transfer Ireland to ensure transparent and consistent procedures for managing Intellectual Property from publicly funded research.

A full description of the Publications cited in the application 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.

5. CTN Business Plan

5.1 Overall Aim

Please state the overall aim of the CTN. The word limit is **100 words**.

5.2 Business Plan

Please provide a high-level Business Plan which will deliver the strategic objectives of the Clinical Trials Network. Include details on staffing resources (to be funded by HRB and other resources) required to deliver the Work Packages (include CTN Director requirements), and percentage time on the job. Please note the Work Package lead in each case.
Provide details on communications approaches with stakeholders (e.g. individual academics/clinicians/allied health professionals, SMEs/ multinationals, cooperative groups or other clinical trial networks).. Please describe anticipated risks to delivery of the award during the proposed term of HRB investment and strategies to mitigate their impact.
The word limit is **600 words**

5.3 Work package details

Please add a small number of clearly-described Work Packages which map to the relevant strategic objectives over the term of the HRB investment 2022-2026. Work Packages should have associated tasks, deliverables and milestones. For each Work Package, deliverables will be used to monitor progress by HRB throughout the lifetime of the award if successful, in addition to agreed performance metrics. Task and deliverables should be mapped against estimated completion timelines in a Gantt chart, and any milestones highlighted.
The word limit is **150 words for each Work Package description, and 200 words for the tasks and deliverables**.

5.4 PERT Chart

Optional upload of a PERT chart which shows how the Work Packages link to the Strategic Objectives of the CTN.

5.5 Gannt Chart

You **must upload a Gantt chart** that lists the above Work Packages, tasks and deliverables against the estimated timelines for completion, together with any additional milestones/key dates (Figure 1).

5.6 Clinical Trial Network Sustainability

Provide an outline 5-year sustainability plan, with **a clear description of the cost-recovery model** to be used for trials and associated activities towards maintaining the network. How will this differ for investigator-led and industry studies? The plan should take into account the need to secure the required additional income to sustain the network beyond the HRB funding period; the expectation for each network as an entity (not the individual members) is to secure €4 – 5 Million in funding for the CTN within the lifetime of the award. The plan should specify suitable potential funding sources to support the clinical trial network throughout and following this award. In each case specify the funding source, specific calls, funding instruments, the level of funding the group could expect to secure (e.g. per award) and the activities that could be covered from such a funding source (e.g. training, funding of a pilot study). In-kind resources (e.g. salary support from institutional sources) should also be described. Targets should be provided for each year, specifying e.g. number of funding applications to be submitted as the Network, and level of funding requested. The word limit is **750 words.**

6. Network Governance and Partnerships

6.1. Network Management and Governance

Please refer to the HRB Clinical Trials and Interventions Research Governance Policy[29]*.* ***Please note that a named Advisory Committee is a minimum requirement of this call***

6.1.1 Add details of the administrative and governance structures that are **currently in place** to manage and provide oversight to the network. Provide terms of reference for these groups, membership and proposed meeting frequency.

6.1.2 Network Management and Governance

(i) Please provide a high-level description of the administrative and governance structures that are **currently in place** to manage and provide oversight to the network. Structures should include the Management Committee, Advisory Committee[30] and if applicable a Stakeholder Advisory Board.

[29] https://www.hrb.ie/fileadmin/1._Non-plugin_related_files/RSF_files/Policies_and_principles/Grant_Policies/HRB_Policy_on_Clinical_Trials_and_Interventions_Governance.pdf

[30] At least one PPI Representative is expected on the Committee, and preferably two

(ii) Describe how the overall governance structure for the CTN will incorporate individual study governance arrangements

(iii) Describe the approach to decision-making for the network, including the approach to strategy development and portfolio development. Clarify how PPI is integrated within portfolio development and prioritisation. Describe the succession plan for the network. Has gender balance been taken into account at decision-making levels? (please refer to HRB's Gender Policy[31]). Does the network follow a Gender policy, or a broader policy on Equality, Diversity and Inclusion?

(iv) Please describe what is working well at present, current challenges, and what will change over the term of investment should this application be successful.

Awardees will also be expected to cooperate fully with any HRB Clinical Trials Infrastructure Expert Advisory Group. This expert advisory group is anticipated to assist HRB in the strategic oversight and performance monitoring of the Infrastructures, Networks, and Interventions portfolio.

The word limit is **1000 words.**

6.1.3 Please upload an organisational chart to illustrate network structure (current and proposed). Please ensure reporting lines of CTN staff are clearly shown.

6.2 Collaborations and Partnerships

Provide a brief summary of your plans for the development of collaborations and partnerships with relevant stakeholders. Give details of any existing or planned collaboration, indicating whether it is a local/regional, national or international activity for a scientific, commercial or policy and practice endeavour.

Any formal collaboration should be documented in the relevant sections of the form (Section 2.4 and 3.3 and supported by a Collaboration Agreement Form or an Infrastructure Agreement Form.)

The word limit is **600 words.**

7. Budget description

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.

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

The maximum total value of an award is €1,000,000 inclusive of overhead contribution.

Overheads will be paid to a maximum of 25% of Total Direct Modified Costs. Overheads are awarded by the HRB to the Host Institution nominated for the award. The apportioning of overheads should be agreed between the partner institutions during the preparation of the application. The HRB expects this to be formalised for successful applications. *If an overhead contribution is requested as part of securing the services of the Clinical Research Infrastructure, it must be included within the overall HRB overhead contribution to the project budget.* It is responsibility of the Principal Investigator, the Host Institution and the Clinical Research Infrastructure provider to establish any sub-agreements as to how the overheads payment from HRB will be distributed in such a case.

Budgets should be broken down using the following budget headings

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 that public sector pay increases up to 1st October 2020 have been published. Please find IUA pay scales at https://www.iua.ie/research-innovation/researcher-salary-scales/. Please apply a salary contingency of 2.0% per annum from 1st Oct 2021. Please note this contingency should be applied cumulatively year on year. **Applicants should include annual pay increments for staff and related costs (pension contribution, employer's PRSI contribution, and overhead contribution) in the budget.** **Note:** The HRB does not provide funding for the salary or benefits of academic staff within research institutions that are already in receipt of salary or benefits. The HRB does not provide salary or buy out time for collaborators
b) Employer's PRSI	Employer's PRSI contribution is calculated at 11.05% for 2020

c) Employer Pension Contribution	Pension provision up to a maximum of 20% of gross salary will be paid to the host institution to enable compliance with the Employment Control Framework (an additional 5% employee contribution is part of the salary). The level of employer contribution should be in accordance with the model adopted by the host institution. If applicable, state the amount of employer contribution based on the pro rata salary and note the % of pro rata salary used to calculate this for reference. Circular Letter 6/2007 states that the pensions contribution of all Public Health Service employees who, on or after 1 June 2007, are granted secondments or periods of special leave with pay to enable them take up appointments with other organisations, including other Public Health Sector organisations, will be increased to 25% of gross pensionable pay. The rate of 25% of gross pensionable pay referred to in this context is the pension contributions to be paid by the body to which the employee is seconded – it does not include any pension contributions which employees make themselves. Where no such arrangements are in place, the HRB will not be liable for costs. If requesting pension costs linked to Circular 6/2007, please provide details as justification for the request.
2. Running Costs	For all general costs of the network, including travel and meetings costs. training, travel costs (including travel bursaries/international exchange visit costs), PPI costs, evidence synthesis costs etc. Hourly costs of experts can be included here. For more substantive contributions by experts, costs should be allocated to salaries. Costs associated with provision of **seed funding** must be presented as a separate budget line. Costs associated with involving members of the **public or patients** in your network e.g. consultation workshops, COS workshops, time spent reviewing material, costs of participation in advisory groups, travel expenses, honoraria, etc. should be charged to running costs. The following costs are ineligible and will not be funded: 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. **We do not expect costs in excess of €10,000 for this call.** Personal/Stand-alone computers will not be funded. All costs must be inclusive of VAT, where applicable.
4. Dissemination Costs	Costs associated with publication of results, seminar/conference attendance (provide details of name and location, where possible) and any other means of communicating/reporting research outcomes as detailed in the dissemination and knowledge exchange plan. Data sharing costs can be included here. Please refer to the HRB policy on Open Access to Published Research[32]. Please list dissemination costs under the following categories: publications, conferences, other activities. **Publications:** Typically, the average HRB contribution towards publication costs is €1,750/per article or **HRB Open Research:** rapid open-peer reviewed and open access platform for all research outputs, with all publication charges covered centrally by the HRB at no expense to the grantee. (www.hrbopenresearch.org) **Conferences:** We envisage that conference costs will be typically around €500 per national conference and €1,500 per international conference.
5. FAIR data Management and Stewardship	Costs related to planning in relation to data management, FAIRification, storage and archiving of research data in line with best practice of data management and stewardship and the FAIR principles **for the proposed studies.** Cost of data management support calculated by hourly rates should also be included here. Please consult Appendix VI of the Guidance Notes for examples of eligible costs.
6. Overhead Contribution	In accordance with the HRB Policy on Overhead Usage, the HRB will contribute to the indirect costs of the network through an overhead payment of **25% of Total Direct Modified Costs** (TDMC excludes student fees, equipment and capital building costs). 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.

7.1 Budget justification and use of resources

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

(i) Please give a clear justification for each position requested, including FTE requirements, salary levels etc.[33] Please set out the proposed role in each case.
These HRB co-funded positions should be clearly identifiable within the organisation chart in section 6.1
(ii). Please clarify any change in each case (e.g. change of funding source, increased time for the role with HRB co-investment, new appointment planned).
(iiI) Please confirm the position of the Network Manager and the funding source (upload Letter of Support as appropriate).
(iv) Demonstrate that HRB funding is not replacing existing financial support from the HI/Hospital/other funding partner.
(v) Please describe how the budget requested from the HRB, plus additional co-investment, are sufficient to successfully deliver the Work Packages. Please explain how good use is made of the budget requested, sharing resources where it is appropriate.

The word limit is **600 words.**

7.2 Upload Letter of Support for Network Manager

This letter, on headed paper and signed by Head of School/Research Centre/Hospital[34], must confirm co-funding for at least 0.5 FTE Network Manager salary for the term of the award. (Please note this co-funding is mandatory for Clinical Trial Networks previously funded by HRB.)

7.3 Other Funding Sources

Please indicate if you have submitted any part of this application, or a similar application, to another HRB scheme or other funding body previously. If this application has been submitted elsewhere, please indicate which HRB scheme or funding body, project title, result of submission or when outcome is expected and the amount of award.
Please note any conflicts of interest which might arise from these funding arrangements. Failure to disclose accurately or fully may result in your application being deemed ineligible and withdrawn without further review. The word limit is **200 words**.

[33] Budget as per HRB budget categories
[34] Depending on the source of the co-funding

Appendix II: References/Useful Links

Study design for interventions

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

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

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

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

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

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

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

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

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

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

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

Studies within a Trial (SWATs)

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

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

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

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

Study registration

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

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

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

Reporting

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

- **EQUATOR Network Library for health research reporting**: an international initiative that seeks to improve reliability and value of health research literature by promoting transparent and accurate reporting of research studies

https://www.equator-network.org/library/

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

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

Clinical Research Infrastructures

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

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

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

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

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

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

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

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

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

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

- **Clinical Research Centre, Royal College of Surgeons in Ireland**

http://www.rcsi.ie/index.jsp?p=331&n=696

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

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

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

Public and Patient Involvement

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

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

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

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

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

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

Data management and sharing and FAIR principles

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

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

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

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

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

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

Gender issues in research

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

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

Evidence synthesis

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

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

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

Appendix III: Trial Oversight Committees

Trial Management Group (TMG)

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

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

Trial Steering Committee (TSC)

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

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

Independent Data Monitoring Committee (IDMC)

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

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

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

Appendix IV: FAIR Data Management

Introduction

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

DMP Requirements

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

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

FAIR Data Management Costs

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

[35] *Please note that not all FAIR data are necessarily open. Where data raises data protection or security concerns, controls and limits on data access will be required. In some cases, it will be appropriate for researchers to delay or limit access to data in order to secure intellectual property protection. Any such restrictions on access should be justified, made explicit via machine-actionable licensing and built-in accessibility protocols mechanisms.*

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

People	Staff time per hour for data collection, data anonymisation,
	staff time per hour for data management/stewardship support, training, etc
Storage and computation	cloud storage, domain hosting charge
Data access	secondary data access, costs for preparing data for sharing (eg anonymisation)
Deposition and reuse	costs for depositing research data and metadata in an open access data repository
	e.g. defining semantic models, making data linkable, choosing the licence, defining metadata for dataset, deploying/publishing
Others	Please further explain
Notes	The HRB is currently not covering the cost of long-term preservation of data

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

Who can help?

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

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