OPEN FUND- LARGE COLLABORATIVE GRANT (OF-LCG)

MAY 2018 GRANT CALL

APPLICATION GUIDE FOR FULL PROPOSAL (FP)

I. OPEN FUND- LARGE COLLABORATIVE GRANT PROGRAMME DETAILS

(A) AIM & FUNDING PRINCIPLES

Aim

The Open Fund- Large Collaborative Grants (OF-LCGs) aim to support the best teams of researchers from public institutions to advance **human health and wellness**, and create **economic value** for Singapore and Singaporeans, through the pursuit of excellence in research and its applications. They represent a unique opportunity to bring together investigators from across all of Singapore with the clinician scientists and clinical investigators in the hospitals and Academic Medical Centres.

Key Elements

- Collaboration within as well as between the basic and clinical research communities is strongly encouraged. Interdisciplinary collaboration across institutions is important to integrate, coordinate and leverage on the full spectrum of research capabilities in Singapore from basic science to clinical research.

- LCG programmes should aim to make significant contributions to the advancement of study of therapeutic areas and help establish Singapore as a global leader.

- They should facilitate the discovery and application of basic science ideas relevant to the advancement of health (as well as the translation of clinical findings into practices and policies if any); and provide opportunities to support industry sectors integral to HBMS economic strategy, namely PharmBio, MedTech, Food & Nutrition and Personal Care. Pathway(s) to impact should be clearly articulated.

Research Themes

The OF-LCG is open to proposals of the highest quality across the breadth of disciplines relevant to its mission. To better realise the goals of Health and Biomedical Sciences (HBMS) in Singapore, the following **five therapeutic areas have been identified as national priorities:**

1. Diabetes Mellitus and Related Metabolic/Endocrine Disorders
2. Infectious Diseases
3. Cardiovascular Diseases
4. Neurological and Sense Disorders
5. Cancers

Themes in these therapeutic areas will be set to focus on issues of particular national interest.

For each grant call, themes will be set in specific therapeutic areas. The HBMS community is encouraged to address these themes. At the same time, proposals in other areas will also be considered. Particularly, the Committee will be keen to consider areas or research technologies that can be developed and applied in more than one disease area, and which can help Singapore advance human health and wellness and create economic value for us.

Grant Call Frequency

Once a year, starting from May 2016.

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May 2018 OF-LCG Grant Call

With effect from the May 2018 grant call, there will be 2 tiers of funding for application:

- **Tier 1 :** up to $10mil inclusive of indirect cost over up to 5 years; and
- **Tier 2** : up to $25mil inclusive of indirect cost over up to 5 years.

Indirect cost is provided at a fixed percentage of 20% of the project's qualifying direct cost.

For the May 2018 OF-LCG grant call, themes will be set in the following 5 therapeutic areas:

1. **Diabetes Mellitus and Related Metabolic/Endocrine Disorders**
2. **Infectious Diseases**
3. **Cardiovascular Diseases**
4. **Neurological and Sense Disorders**
5. **Cancers**

The tables below list the details of the set themes.

1. DIABETES MELLITUS AND RELATED METABOLIC/ENDOCRINE DISORDERS

Set themes	Focus area and challenge statement
Primary Prevention of Diabetes.	**Focus area:** To address the rising incidence of diabetes and the relatively large number of Singaporeans who have diabetes but are not aware of it. **Challenge statement:** To utilise basic, clinical, public health and translational research to develop an effective diabetes prevention programme. This is in support of national goals to reduce the incidence of diabetes by 20% by 2030, reduce the proportion of undiagnosed diabetes by 30% (currently 50%) by 2025 and reduce the progression of gestational diabetes to Type 2 Diabetes by 30% by 2025.

2. INFECTIOUS DISEASES

Set themes	Focus area and challenge statement
Infectious Diseases including pandemic/ Emerging Infectious Diseases (EID) (e.g. Respiratory Tract Infection (RTI), Antimicrobial Resistance & healthcare-associated infection, Dengue & vector control)	**Focus area:** Determining and breaking the development of transmission and/or resistance chain. **Challenge statement:** To utilise basic, clinical, public health and translational research to build capabilities to understand the factors influencing the transmission and to develop measures for early detection, prevention of transmission and control of the diseases. This will support the national goal in reducing the ID case counts and their associated socioeconomic costs for Singapore.

3. CARDIOVASCULAR DISEASES

Set themes	Focus area and challenge statement
Macrovascular Diseases: Myocardial infarction and chronic coronary heart disease, Stroke or Aortic and Peripheral Arterial Disease	**Focus area:** To better understand, delay the onset and reduce complications of macrovascular diseases **Challenge statement:** To utilise basic, translational, clinical and implementation science approaches to improve the understanding of basic mechanisms that contribute to the origin and complications of macrovascular diseases as well as identify targets and ways to mitigate them. Due consideration should be given to the cost-effectiveness of the approaches, and the attractiveness of such approaches to industry. This is in support of long-term goals in Myocardial infarction and chronic coronary heart disease *on* • delaying the average age of onset of acute coronary syndromes and acute heart failure events by 5 years within the next 5-10 years; • reducing 30-days post-MI mortality by 30% over the next 5 years and • doubling survival from Out-of-Hospital Cardiac Arrest over the next 5 years from 11% to 22%. Stroke *on* reducing the incidence of stroke by 20% in 10 years; • reducing mortality and morbidity from stroke by 20%. Aortic and Peripheral Arterial Disease *on* • delaying the average age of onset of aortic and peripheral artery disease by 5 years within the next 5-10 years; • reducing the number of surgical arterial interventions required for macrovascular disease by 20% within the next 10 years, and • establishing accurate documentation of the disease burden. These goals are also aided by efforts from MOH and healthcare institutions to promote screening of CVD risk factors (e.g. hypertension, diabetes, BMI, sex, age, obesity, diet, lipids) from age 40 in Singapore.

4. NEUROLOGICAL AND SENSE DISORDERS

Set themes	Focus area and challenge statement

Age-related neurological and eye disorders (e.g. Vascular Dementia, Parkinson's Disease, Glaucoma)	**Focus area:** To improve disease diagnosis, reduce incidence and progression and develop new therapies to enhance quality of life from age-related neurological and eye disorders **Challenge statement:** To utilise basic, translational, clinical and implementation science approaches to improve the understanding of basic mechanisms behind age-related neurological and eye disorders so as to improve disease diagnosis, reduce incidence and progression, and develop new therapies that enhance quality of life. Due consideration should be given to the cost-effectiveness of the approaches, and the attractiveness of such approaches to industry. This is in support of long-term goals of (i) reducing the disease burden and hospital readmission rate of age-related neurological disorders by 10-20% in 10 years; (ii) reducing the prevalence of age-related blindness and vision loss by 20% within 10 years in the national population, and reducing complications of eye diseases by 20% within 10 years in the at-risk population in Singapore.

5. CANCERS

Set themes	Focus area and challenge statement
Precision Methods for prevention, disease detection and treatment stratification, (e.g. in Breast cancer, Gastrointestinal (colorectal & gastric) cancer, Haematological cancer, Liver cancer, Nasopharyngeal cancer)	**Focus area:** To reduce preventable cancers and optimise treatment for cancer patients in Singapore **Challenge statement:** To utilise basic, translational, clinical and implementation science approaches to enable the identification of at-risk individuals, early detection of cancer and stratification of cancer treatment (e.g. through the identification of biomarkers). Due consideration should be given to the cost-effectiveness of the approaches, and the attractiveness of such approaches to industry. This is in support of long-term goals of reducing the national incidence of late-stage cancer by 10% by 2025, and increasing the survival rate of cancer patients in Singapore by 20% by 2030.
Metastasis and Resistance (e.g. in Breast cancer, Gastrointestinal (colorectal & gastric) cancer, Haematological cancer, Liver cancer, Nasopharyngeal cancer)	**Focus area:** To develop novel understandings of and therapy for Asia-prevalent cancers **Challenge Statement:** To utilise basic, translational, clinical and implementation science approaches to understand the major factors mediating drug resistance and metastasis, and develop novel therapy to mitigate them so as to improve the survival of cancer patients. Due consideration should be given to the cost-effectiveness of the approaches, and the attractiveness of such approaches to industry. This is in support of the long-term goal of increasing the survival rate of cancer patients in Singapore by 20% by 2030.

Enhancing Cancer Immunotherapy, (e.g. in Breast cancer, Gastrointestinal (colorectal & gastric) cancer, Haematological cancer)	**Focus area:** To improve outcomes of Asia-prevalent cancers using immunotherapies **Challenge Statement:** To utilise basic, translational, clinical and implementation science approaches to improve patient selection for immunotherapy, so that patients receive maximum benefit from the therapy (e.g. through the development of new targets for immunotherapy or overcoming resistance). Due consideration should be given to the cost-effectiveness of the approaches, and the attractiveness of such approaches to industry. This is in support of the long-term goal of increasing the survival rate of cancer patients in Singapore by 20% by 2030.

(B) Definitions and Eligibility Criteria

Definitions

Overview: The research programme should comprise no more than 5 research themes, each led by one or more Theme Principal Investigators (PIs). All the Theme PIs should form the Leadership Team, and one of the Theme PIs should be nominated as the Corresponding PI.

Leadership Team: Comprises all Theme PIs. The leadership team share the responsibility in making the OF-LCG programme a success and is essential for implementing programme strategies and achieving desired outcomes.

Corresponding PI: The Theme PI who will coordinate the OF-LCG programme, serve as the main point of contact between NMRC and the OF-LCG Leadership Team, and is accountable to NMRC for the proper conduct of the whole programme. He/ She will work closely with the Theme PIs to resolve any issues which arise during the course of the programme, including the usage of funding, any variations to the scope of the programme etc.. Limited to only 1 Corresponding PI per leadership team.

Theme PI: Theme PIs have the responsibility to direct each specific research theme being supported by the grant, and accountable for the proper conduct of the specific research theme. There is no limit on the no. of Theme PIs per theme but a cap of 5 themes applies. An individual can be a Theme PI for multiple themes. The main Theme PI is responsible for the collation and submission of requisitions for direct and/or indirect costs, on behalf of the theme to NMRC for the disbursement of funds. There is only one main Theme PI to be nominated per theme.

Eligibility Criteria

- **Only one Corresponding Principal Investigator (PI) is allowed per application, and there is no cap placed on the number of Theme PIs per theme. However, a cap of 5 themes applies.**

- **The Corresponding PI and Theme PIs form the Leadership Team and are required to fulfil the following criteria at the point of application:**

i. Holds a primary appointment in a local publicly funded institution and salaried by the institution.
ii. Has PhD or MD/MBBS/BDS qualifications (exceptions would be made on a case-by-case basis).
iii. Is an independent PI with a demonstrated track record of research, as evidenced by the award of nationally competitive funding (international funding to be considered on a case by case basis), substantial publication record in the past 3 years, or PI status in research institutes.
iv. Has a laboratory or clinical research program that carries out research in Singapore.
v. Holds a minimum of 9 months employment (per calendar year) with local Singapore institution(s). Upon award, the PI must agree to fulfil at least 6 months of residency in Singapore for each calendar year over the duration of the grant award.
vi. Has no outstanding report from previous BMRC, NMRC grants, and other national grants.
vii. For proposals involving patients, the PI should be SMC registered; or should be able to demonstrate ability to access patients through SMC registered Co-Is or collaborators.

(C) Funding Quantum and Duration

Up to $10mil (Tier 1) or $25mil (Tier 2) per project over up to 5 years, amount is inclusive of indirect cost provided at a fixed percentage of 20% of the project's qualifying direct cost.

(D) Review Process

Overview

The OF-LCG comprises a 2-stage review process. In the first stage, interested applicants are required to submit a letter of Intent (LOI). The LOIs solicited will be put through an internal review process with the OF-LCG Review Panel (OF-LCGRP) that is made up of local and international clinicians and basic scientists, as well as industry experts appointed by NMRC. Based upon a review and selection of the most promising projects, a certain number of applicants will be invited to submit full proposals.

In the second stage, the full proposals will be evaluated by international domain experts followed by OF-LCG Review Panel (OF-LCGRP). Shortlisted applicants will be invited to submit a rebuttal to address the issues raised by the international reviewers, and will subsequently be interviewed by the OF-LCGRP. The OF-LCGRP will do a collective review/ranking of the proposals and make funding recommendations to the OSFC-select for endorsement. The number of awards given out for the grant call will depend on the quality of the proposals and the amount of funding available.

Selection Criteria

Selection of successful proposals would be based on the following evaluation criteria:

i. High-quality scientific research spanning basic science to clinical translation.
ii. Proposed research topic should address issues of national importance. These should typically be challenges that no single institution or discipline can solve and require collaborative and interdisciplinary approaches. Provided they are scientifically meritorious, proposals which address the set themes in the therapeutic areas would be given priority consideration.
iii. Proposed research must be well-differentiated and highly competitive. It should demonstrate a high potential to be world class.
iv. Demonstrate the potential to improve **health outcomes** and capture **economic value*** with a clear indication of pathway(s) to impact.

An ***industry engagement plan will be required in the application, and applicants are encouraged to obtain ***letters of support from the industry***.*

(E) Reporting Requirements

Reporting requirements are detailed in NMRC's Terms and Conditions and Guidelines for the Management of MOH/NMRC (Grantor) Funding Programmes (available on NMRC's website).

In addition, research programmes funded under the OF-LCG may be required to undergo an annual review of their progress by an NMRC-appointed Scientific Advisory Board (SAB) and mid-term reviews by an appointed Review Panel. More details will be shared with the grantees at the start of their research programme.

(F) Terms & Conditions

If awarded, all applicants would have read, understood and will abide to **NMRC's Terms and Conditions and Guidelines for the Management of MOH/NMRC (Grantor) Funding Programmes** (available on NMRC's website) upon their acceptance of the grant.

II. GENERAL INSTRUCTIONS

- Please provide both MS word doc format for all attachments on IGMS (except for Section 6).

- Use **Arial font size 10** for all text and attachments. Please follow the instructions for each section closely.

- For identification purposes, please indicate the name of the Corresponding PI and host institution in the header of the respective templates.

- **The Corresponding PI and Theme PIs must fulfill the eligibility criteria specified in Section I of this application guide.** Please note that in IGMS, the Corresponding PI will take on the role of "Lead PI". The main Theme PI[1] will take on the role of "Team PI". The other Theme PIs will take on the role of "Co-Is" and their Theme PI roles for the respective themes is to be indicated in the 'remarks column' on the individual profile page.

- **Each application is limited to only 1 Corresponding PI. No cap is placed on the number of Theme PIs allowable per theme. A Corresponding PI must be a Theme PI. An individual can be a Theme PI for more than 1 theme. A cap of 5 themes per application applies.**

- **Co-Is[2] are required to hold at least an adjunct position at a local public institution. Researchers from overseas institutions or private companies can only participate as Collaborators[3].** The terms of collaboration with overseas research institutions and private companies must conform to NMRC's existing policies.

- There is no limit to the number of Co-Investigators (Co-Is) or Collaborators. **Please list and specify/ describe the roles of Co-Investigators and Collaborators in the relevant section(s).**

- **The page limit for the CVs of the Corresponding PI and Theme PIs is 3 pages; while the page limit for the CVs of the Co-Is and Collaborators is 2 pages.** Please indicate "NA" if the required information is not applicable and note that NMRC will not be responsible for any missing information not provided in the CV.

- **Please note that resubmission attempts are capped at up to two times. Funding is not guaranteed for resubmitted proposals.**
  Note: resubmission refers to proposals resubmitted based on the OF-LCGRP/ External Reviewers' comments. It is not a re-written proposal from a new perspective. If more than 50% of the proposal is to be revised, it should be submitted as a new application.

- Plagiarism (without permission from author or reference made to source) will be referred to Host Institution for investigation and may be subjected to disciplinary actions.

- Refer to **Appendix 1** of this document for the checklist on Study Design and Statistical Considerations to help complete Section 1.2(v)- "Methods"- of the application form.

[1] **Theme PI**: An individual with the responsibility to direct each specific research theme being supported by the grant, and accountable for the proper conduct of the specific research theme.
[2] **Co-I:** An individual involved in the scientific development and execution of the project. A co-Investigator typically devotes a higher percentage of effort to the project compared to a collaborator and is considered a key research personnel of the research team.
[3] **Collaborator:** An individual involved in the scientific development and execution of project. A collaborator typically devotes only a specific percentage of effort to the project.

DEFINITIONS

Overview: The research programme should comprise no more than 5 research themes, each led by one or more Theme Principal Investigators (PIs). All the Theme PIs should form the Leadership Team, and one of the Theme PIs should be nominated as the Corresponding PI.

Leadership Team: Comprises all Theme PIs. The leadership team share the responsibility in making the OF-LCG programme a success and is essential for implementing programme strategies and achieving desired outcomes.

Corresponding PI: The Theme PI who will coordinate the OF-LCG programme, serve as the main point of contact between NMRC and the OF-LCG Leadership Team, and is accountable to NMRC for the proper conduct of the whole programme. He/ She will work closely with the Theme PIs to resolve any issues which arise during the course of the programme, including the usage of funding, any variations to the scope of the programme etc. Limited to only 1 Corresponding PI per leadership team. *Please note that in IGMS, the Corresponding PI will take on the role of "Lead PI".*

Theme PI: Theme PIs have the responsibility to direct each specific research theme being supported by the grant, and accountable for the proper conduct of the specific research theme. There is no limit on the no. of Theme PIs per theme but a cap of 5 themes applies. An individual can be a Theme PI for multiple themes.

Co-Investigator (Co-I): An individual involved in the scientific development and execution of the project. A co-Investigator typically devotes a higher percentage of effort to the project compared to a collaborator and is considered a key research personnel of the ***"Research Team"***. He/ She is required to hold at least an adjunct appointment at a local public institution. There is no limit on the no. of participating co-Is.

Collaborator: An individual involved in the scientific development and execution of project. A collaborator typically devotes only a specific percentage of effort to the project. Researchers from overseas institutions or private companies can only participate as collaborators as well. There is no limit on the no. of participating collaborators.

Administrative core: A team of people involved in the administration of the programme, e.g. programme manager etc. They are fundable under direct cost and their roles include:

- Overseeing and managing the programme's administrative matters and activities.
- Reporting directly to the Corresponding PI.
- Liaising with NMRC and other external agencies regarding any programme or grant matters**.**

III. REQUIRED SECTIONS OF THE FP APPLICATION

<table>
<tr><th>SECTION</th><th>DESCRIPTION</th></tr>
<tr><td>-</td><td>Summary Details</td></tr>
<tr><td>1</td><td>Research Proposal
i) Sub-section 1.1 (page limit of 3)
ii) Sub-section 1.2 i, iii, iv & v (page limit of 4 pages per theme)
iii) Sub-section 1.3 (page limit of 5)
iv) Sub-section 1.4 (page limit of 2)
v) Sub-section 1.5 (page limit of 14)</td></tr>
<tr><td>2</td><td>Curriculum Vitae of the Corresponding and Theme PIs (page limit: 3 per CV); and Co-Investigators and Collaborators (page limit: 2 per CV)</td></tr>
<tr><td>3</td><td>Industry Parties' Contributions and Other Support</td></tr>
<tr><td>4</td><td>Expected Outcomes</td></tr>
<tr><td>5</td><td>Annexes
<table>
<tr><th>Annex</th><th>Description</th></tr>
<tr><td>Annex A (max. 5 pages)</td><td>Additional documents for RENEWAL applications:
• Summary of achievements of the last funding and if they met the aims and objectives of the previous research programme. Explain unmet goals.
• Brief description of plans laid out for the new tranche of funding and how it is a progression from the last funding.</td></tr>
<tr><td>Annex B</td><td>Additional documents for RENEWAL applications:
• Final/ progress report</td></tr>
<tr><td>Annex C (max. 2 pages)</td><td>Additional documents for RESUBMISSION applications:
• Summary of how the revised proposal (i.e. the re-submission application) has addressed past reviewers'/panel's comments, and highlight new features and merits of the revised proposal</td></tr>
<tr><td>Annex D</td><td>Additional documents for RESUBMISSION applications:
• Reviewers' report of previous unsuccessful application; Rebuttal to the external reviewers; Panel's comments (where applicable); and Response to the panel (where applicable)</td></tr>
<tr><td>Annex E</td><td>Research Team Summary and References</td></tr>
<tr><td>Annex F</td><td>Budget Summary</td></tr>
<tr><td>Annex G</td><td>Scientific abstracts of all grants listed in Section 3; for NMRC funded projects, include latest research outcomes/ KPIs achieved</td></tr>
<tr><td>Annex H</td><td>Industrial-partnered entities' supporting document on commercialisation potential & Industry support letters (if any)</td></tr>
</table></td></tr>
<tr><td>6</td><td>Declaration and Signatories to be submitted as a separate document from the preceding sections 3-5.</td></tr>
</table>

APPLICATION SUBMISSION

- All attachments (except Section 6) must be uploaded in word doc format. Applications be submitted by the Corresponding PI and endorsed by the Corresponding PI's Host Institution through IGMS by **2 October 2018 (Tue), 5pm**.

- Internal Host Institution submission deadline may apply, please check with your Research Office for more information.

- The following will be rejected:

    - Incomplete applications e.g. missing documents such as re-submission materials required and missing progress/ final reports for renewal applications, missing signatures, sections left blank, missing CVs, etc.

    - Outdated application templates.

- No late submission or revision to the submitted application will be entertained after the closing date.

- For enquiries, please contact the NMRC OF-LCG secretariat at Gillian_Neo@moh.gov.sg or Rane_Tan@moh.gov.sg.

IV. QUICK GUIDE TO APPLICATION VIA IGMS

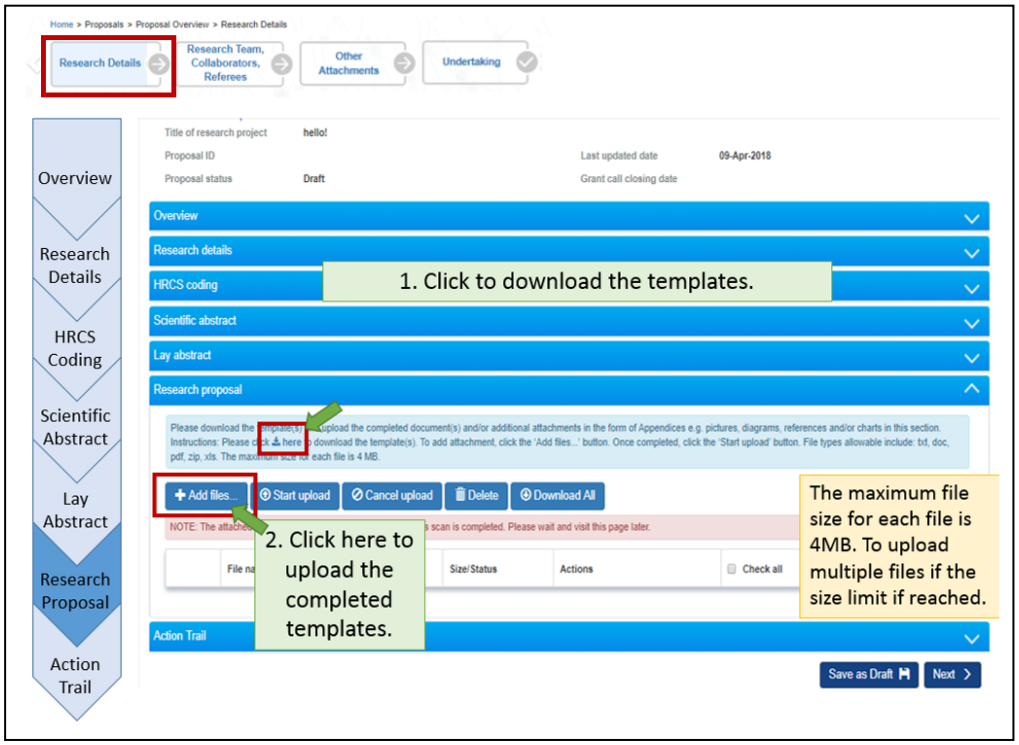
The application will comprise a "Summary Details" section and 6 additional sections, as shown at the table on Pg 12.

Templates to Download

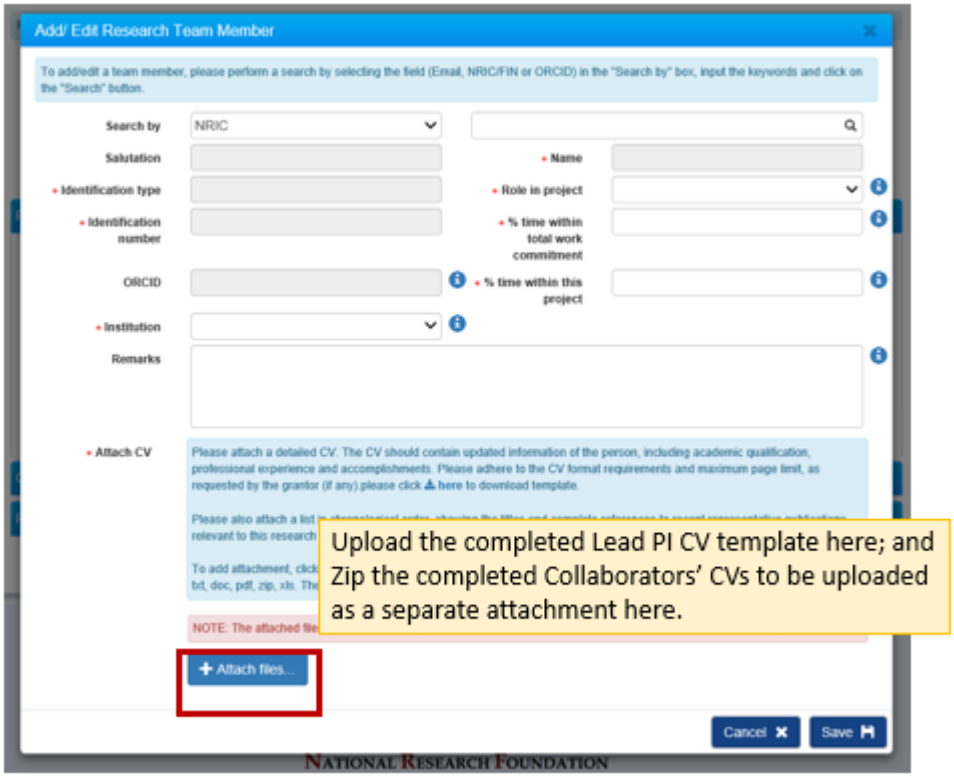
- The templates for **Summary Details,Sections 1,3 to 6** can be downloaded from the "***Research Proposal***" tab of the "***Research Details***" section.
- The templates for **Section 2** (CV) can be downloaded from "***Research Team***" tab of the "***Research Team***" section.

Documents to Upload

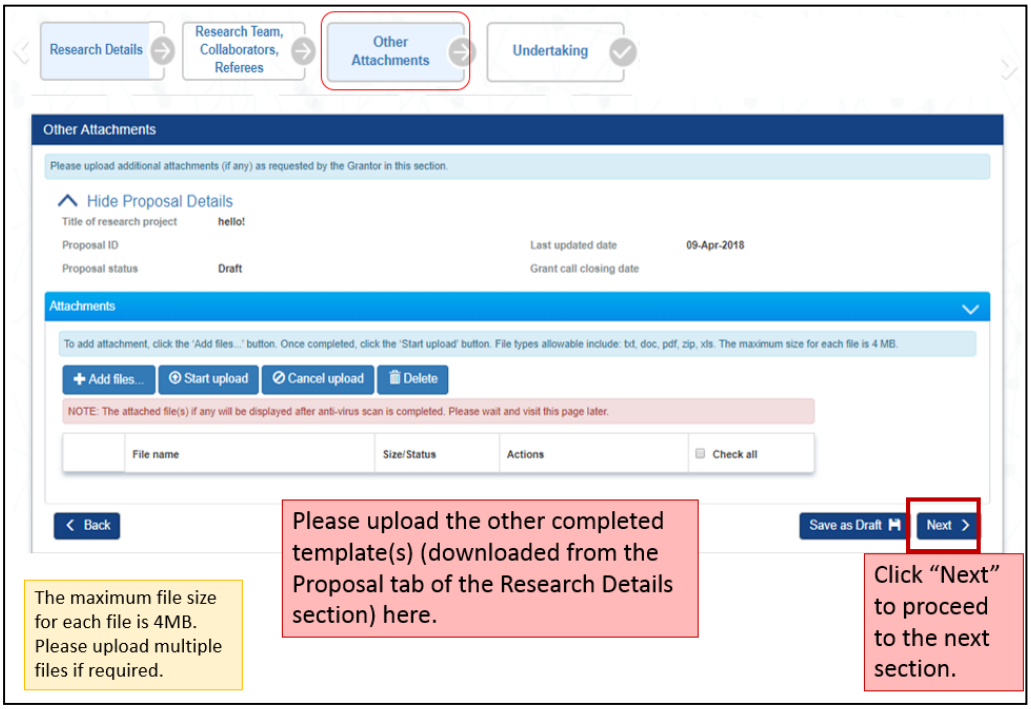
- Completed **Summary Details** (Section 0) and **Section 1** templates are to be uploaded as 2 separate documents into "***Research Proposal***" tab of the "***Research Details***" section.



- Completed **Section 2** templates for the Corresponding PI, Theme PI and Co-Is are to be uploaded into the respective profiles of the Corresponding PI, Theme PI and Co-I under the "***Research Team***" tab of the "***Research Team, Collaborators, Referees***" section.
- Completed **Section 2** templates for the Collaborators are to combined into a zip file to be uploaded alongside the Lead PI's CV in the Lead PI's profile under the "***Research Team***" section.



- Completed **Sections 3-6** are to be uploaded into the "***Other Attachments***" section as separate files.



HEALTH RESEARCH CLASSIFICATION SYSTEM

The Health Research Classification System is a bespoke system for classifying the full spectrum of biomedical and health research - from basic to applied - across all areas of health and disease. It was developed by the UK Clinical Research Collaboration Partners. It is supported by an online reference source and manual - "http://www.hrcsonline.net/".

Health Categories

Category	Includes
Blood	Haematological diseases, anaemia, clotting and normal development and function of platelets and erythrocytes
Cancer	All types of cancers (includes leukaemia)
Cardiovascular	Coronary heart disease, diseases of the vasculature and circulation including the lymphatic system, and normal development and function of the cardiovascular system
Congenital Disorders	Physical abnormalities and syndromes that are not associated with a single type of disease or condition including Down's syndrome and cystic fibrosis
Ear	Deafness and normal ear development and function
Eye	Diseases of the eye and normal eye development and function
Infection	Diseases caused by pathogens, acquired immune deficiency syndrome, sexually transmitted infections and studies of infection and infectious agents
Inflammatory and Immune System	Rheumatoid arthritis, connective tissue diseases, autoimmune diseases, allergies and normal development and function of the immune system
Injuries and Accidents	Fractures, poisoning and burns
Mental Health	Depression, schizopnrenia, psychosis and personality disorders, addiction, suicide, anxiety, eating disorders, learning disabilities, autistic spectrum disorders and studies of normal psychology, cognitive function and behavior
Metabolic and Endocrine	Diabetes, thyroid disease, metabolic disorders and normal metabolism and endocrine development and function
Musculoskeletal	Osteoporosis, osteoarthritis, muscular and skeletal disorders and normal musculoskeletal and cartilage development and function
Neurological	Dementias, transmissible spongiform encephalopathies, Parkinson's disease, neurodegenerative diseases, Alzheimer's disease, epilepsy, multiple sclerosis and studies of the normal brain and nervous system
Oral and Gastrointestinal	Inflammatory bowel disease, Crohn's disease, diseases of the mouth, teeth, oesophagus, digestive system including liver and colon, and normal oral and gastrointestinal development and function
Renal and Urogenital	Kidney disease, pelvic inflammatory disease, renal and genital disorders, and normal development and function of male and female renal and urogenital system
Reproductive Health and Childbirth	Fertility, contraception, abortion, *in vitro* fertilisation, pregnancy, mammary gland development, menstruation and menopause, breast feeding, antenatal care, childbirth and complications of newborns
Respiratory	Asthma, chronic obstructive pulmonary disease, respiratory diseases and normal development and function of the respiratory system
Skin	Dermatological conditions and normal skin development and function
Stroke	Ischaemic and haemorrhagic
Generic Health Relevance	Research applicable to all diseases and conditions or to general health and wellbeing of individuals. Public health research, epidemiology and health services research that is not focused on specific conditions. Underpinning biological, psychosocial, economic or methodological studies that are not specific to individual diseases or conditions
Other	Conditions of unknown or disputed aetiology (such as chronic fatigue syndrome! myalgic encephalomyelitis), or research that is not of generic health relevance and not applicable to specific health categories listed above

Overview of the Research Activity Codes

1	**Underpinning Research**
1.1	Normal biological development and functioning
1.2	Psychological and socioeconomic process
1.3	Chemical and physical sciences
1.4	Methodologies and measurements
1.5	Resources and infrastructure (underpinning)
2	**Aetiology**
2.1	Biological and endogenous factors
2.2	Factors relating to physical environental
2.3	Psychological, social and economic factors
2.4	Surveillance and distribution
2.5	Research design and methodologies
2.6	Resources and infrastructure
3	**Prevention of Disease and Conditions, and Promotion of Well-Being**
3.1	Primary prevention interventions to modify behaviours or promote well-being
3.2	Interventions to alter physical and biological environmental risks
3.3	Nutrition and chemoprevention
3.4	Vaccines
3.5	Resources and infrastructure (prevention)
4	**Detection, Screening and Diagnosis**
4.1	Discovery and preclinical testing of markers and technologies
4.2	Evaluation of markers and technologies
4.3	Influences and impact
4.4	Population screening
4.5	Resources and infrastructure (detection)
5	**Development of Treatments and Therapeutic Interventions**
5.1	Pharmaceuticals
5.2	Cellular and gene therapies
5.3	Medical devices
5.4	Surgery
5.5	Radiotherapy
5.6	Psychological and behavioural
5.7	Physical
5.8	Complementary
5.9	Resources and infrastructure (development of treatments)
6	**Evaluation of Treatments and Therapeutic Interventions**
6.1	Pharmaceuticals
6.2	Cellular and gene therapies
6.3	Medical services
6.4	Surgery
6.5	Radiotherapy
6.6	Psychological and behavioural
6.7	Physical
6.8	Complementary
6.9	Resources and infrastructure (evaluation of treatments)
7	**Management of Diseases and Condition**
7.1	Individual care needs
7.2	End of life care
7.3	Management and decision making
7.4	Resources and infrastructure (disease management)
8	**Health and Social Care Services Research**
8.1	Organisation and delivery of services
8.2	Health and welfare economics
8.3	Policy, ethics and research governance
8.4	Research design and methodologies
8.5	Resources and infrastructure (health services)

Research Activity Codes

1. Underpinning Research	**Research that underpins investigations into the cause, development, direction, treatment and management of diseases, conditions and ill health**
1.1 Normal biological development and functioning	Studies of normal biology including - genes and gene products - molecular, cellular and physiological structures and function - biological pathways and processes including normal immune function - developmental studies and normal ageing - bioinformatics and structural studies - development and characterisation of model systems
1.2 Psychological and socioeconomic process	Studies that do not address health directly but cover issues that may have a bearing on health and well-being including - perception, cognition and learning processes - social and cultural beliefs - individual or group characteristics and behaviours - politics, economies and urban development - development and characterisation of model systems
1.3 Chemical and physical sciences	Research in chemical and physical sciences that may lead to the future development of diagnostic tools or medical treatments including - bioengineering and biophysics - chemical structures, interactions and properties - molecular modelling - material science
1.4 Methodologies and measurement	Development of novel underpinning research measures and analytical methodologies including - development of statistical methods and algorithms for genomic analysis - development of mapping methodologies and novel data comparison methods - development of biological, psychological and socioeconomic research measures
1.5 Resources and infrastructure (underpinning)	- development and/or distribution of resources for use by the research community including equipment, cell lines, DNA banks, and genomic and proteomic sequence resources - infrastructure to support research networks, consortia and centres

Research Activity Codes

2 Aetiology	**Identification of determinants that are involved in the cause, risk or development of disease, conditions and ill health**
2.1 Biological and endogenous factors	Identification and characterisation of endogenous factors known or suspected to be involved in the cause, risk or development of disease, conditions or ill health including - genes and gene products, molecular, cellular and physiological structures and functions - biological factors linked to ethnicity, age, gender, pregnancy and body weight - endogenous biological factors or pathways involved in responses to infection or damage by external factors - metastases, degenerative processes, regeneration and repair - complications, reoccurrence and secondary conditions - bioinformatics and structural studies - development and characterisation of models
2.2 Factors relating to physical environment	Environmental or external factors associated with the cause, risk or development of disease, conditions or ill health including - physical agents, occupational hazards, environmental surroundings, radiation and pollution - chemicals and nutrients - infection by pathogens and studies of infectious agents
2.3 Psychological, social and economic factors	Research into psychological conditions, or research into the cause, risk or development of disease, conditions or ill health associated with social, psychological and economic factors including - individual or group behaviours and lifestyle - cultural or religious beliefs or practices - ethnicity, age and gender differences - socioeconomic factors
2.4 Surveillance and distribution	Observational studies, surveys, registries. and studies that track incidence, prevalence, morbidity, co-morbidity and mortality including ongoing monitoring of large scale cohorts
2.5 Research design and methodologies (aetiology)	Development of aetiological and epidemiological research designs, measures and methodologies including - methodological innovation and modelling complex epidemiological data - development and evaluation of novel research designs - development of epidemiological research measurements includingoutcome measures - development of analytical and statistical methods to understand disease cause, susceptibility and risk including genetic linkage and association studies
2.6 Resources and infrastructure (aetiology)	- development and/or distribution of resources for general use by the research community including equipment, cell lines, tissue and DNA banks, and genomic and proteomic sequence resources - infrastructure to support research networks, consortia and centres

Research Activity Codes

3 Prevention of Disease and Conditions, and Promotion of Well-Being	**Research aimed at the primary prevention of disease, conditions or ill health, or promotion of well-being**
3.1 Primary prevention interventions to modify behaviours or promote well-being	Development, implementation and evaluation of interventions to modify personal or group behaviours and lifestyles affecting health and well-being including - risk behaviours associated with diet, tobacco use, physical activity, alcohol consumption, sexual health and substance misuse - age, gender, cultural or religious practices - public health policy, health communication and educational interventions - behavioural, psychological, social and physical interventions
3.2 Interventions to alter physical and biological environmental risks	Development, implementation and evaluation of interventions surrounding physical, biological and environmental risk factors including - radiation, second-hand smoke, physical and chemical agents, - occupational hazards and environmental surroundings - contraceptive devices - infectious agents - policy, educational and physical interventions
3.3 Nutrition and chemoprevention	Research on chemopreventative agents and health protective effects of nutrients including - development, characterisation and mechanism of action - chemical contraceptives - testing and evaluation in model systems and clinical, applied and community settings - evaluation of evidence to inform policy
3.4 Vaccines	Research on vaccines for prevention of disease including - discovery, development and testing of vaccines and vaccination in model systems - mechanism of action - development, implementation and evaluation of vaccination programmes and studies to increase uptake - decision making, outcomes from vaccination and evaluation of evidence to inform policy
3.5 Resources and infrastructure (prevention)	- development and/or distribution of resources for use by the research community including equipment, ceil lines, tissue and DNA banks - infrastructure to support research trials, networks, consortia and centres

Research Activity Codes

4 Detection, Screening and Diagnosis	**Discovery, development and evaluation of diagnostic, prognostic and predictive markers and technologies**
4.1 Discovery and preclinical testing of markers and technologies	Discovery, development and preclinical testing of novel markers (that may be derived from patient samples) and technologies for use in detection, diagnosis, prediction, prognosis and monitoring including - biological and psychological markers - diagnostic and monitoring devices, imaging, scanning, predictive and - diagnostic tests - development and characterisation of models - diagnostic measures and methodologies
4.2 Evaluation of markers and technologies	Testing and evaluation of markers and technologies in humans for use in detection, diagnosis, prediction, prognosis and monitoring in clinical, community or applied settings including - assessment of sensitivity, efficacy, specificity. predictive and prognostic value, reproducibility and safety - medical devices, imaging, diagnostic and predictive tests - evaluation of diagnostic models, methods and methodologies in clinical or applied settings
4.3 Influences and impact	Studies investigating impact of screening and factors affecting uptake including - attitudes and beliefs including cultural and religious practices - issues relating to gender, age and ethnicity - genetic counselling and decision making - psychological, social and economic factors - development, implementation and evaluation of interventions to promote screening including policy, education and communication
4.4 Population screening	Studies investigating population screening programmes including - feasibility studies, pilot studies and trials - evaluation of effectiveness, benefits and economic evaluation - impact on health services and policy issues - models of population surveillance
4.5 Resources and infrastructure (detection)	- development and/or distribution of resources for use by the research community including equipment, cell lines, tissue and DNA banks, and informatics systems - infrastructure support for research trials, networks, consortia and centres

Research Activity Codes

5 Development of Treatments and Therapeutic Interventions	**Discovery and development of therapeutic interventions and testing in model systems and preclinical settings**
5.1 Pharmaceuticals	Identification and development of pharmaceutical small molecules, therapeutic vaccines, antibodies and hormones including - drug screening and development of delivery systems - mechanism of action including side effects and drug resistance - pharmacogenetics, prediction of genetic variation and responses to drugs - testing in in vitro and in vivo model systems
5.2 Cellular and gene therapies	Discovery and development of cellular, tissue and gene therapies including - gene therapy, stem cells therapy, in vitro fertilisation and tissue engineering - development of delivery systems - development of culture systems - testing in in vitro and in vivo model systems
5.3 Medical devices	Discovery and development of medical devices including - implantable devices, mobility aids, dressings, medical equipment and prostheses - biological safety assessments and investigation of adverse events - sterilisation and decontamination of equipment or surfaces - testing in in vitro and in vivo model systems
5.4 Surgery	Development of surgical, obstetric and dental interventions including - histocompatability, transfusions, transplantations including xenograft studies and bone marrow transplants - mechanisms of recovery, tolerance, rejection and side effects including infection - testing in in vitro and in vivo model systems
5.5 Radiotherapy	Discovery and development of interventions including - radiobiology, radiotherapy, radioimmunotherapy, radiosensitisers, microwaves, ultrasound, laser and phototherapy - development of delivery systems - investigation of mechanisms of action and side effects - testing in in vitro and in vivo model systems
5.6 Psychological and behavioural	Development of psychological and behavioural interventions including - cognitive behavioural therapy, electro-convulsive therapy, counselling, therapy and social interventions - testing in model systems
5.7 Physical	Development of physical interventions including - physical therapies, physiotherapy, occupational therapy, speech therapy, dietetics, exercise and osteopathy - mechanisms of action - testing in model systems
5.8 Complementary	Discovery and development of complementary approaches to conventional medical therapies including - hypnotherapy, meditation, massage, acupuncture and homeopathy - mechanisms of action - testing in model systems

Research Activity Codes

6 Evaluation of Treatments and Therapeutic Interventions	**Testing and evaluation of therapeutic interventions in clinical community or applied settings**
5.9 Resources and infrastructure (development of treatments)	▪ development and/or distribution of resources for general use by the research community including equipment, cell lines, tissue and DNA banks ▪ infrastructure support for networks, consortia and centres
6.1 Pharmaceuticals	Clinical application and evaluation of pharmaceutical small molecules, therapeutic vaccines, antibodies and hormones in humans including ▪ small scale settings and pilot studies ▪ phase I, II, III and IV trials ▪ assessing sensitivity, efficacy, specificity, relapse, survival, therapeutic value, pharmacokinetics, reproducibility and safety ▪ studies monitoring response, outcome, drug resistance and side effects
6.2 Cellular and gene therapies	Clinical application and evaluation of cellular, tissue and gene therapies in humans including ▪ small scale and pilot studies ▪ phase I, II, III and IV trials ▪ gene therapy, stem cell therapy, in vitro fertilisation, tissue engineering ▪ evaluation of applied delivery systems
6.3 Medical devices	Application and evaluation of medical devices in humans in a clinical, community or applied setting including ▪ implantable devices, mobility aids, dressings, medical equipment and prostheses ▪ validation of design and post market surveillance
6.4 Surgery	Clinical and applied application and evaluation of surgical, obstetric and dental interventions in humans including ▪ small scale and pilot studies ▪ phase I, II, III and IV trials ▪ procedures including organ and bone marrow transplantation, tissue grafts and transfusions ▪ monitoring outcomes, side effects and rejection
6.5 Radiotherapy	Clinical application and evaluation of interventions in humans including ▪ small scale and pilot studies ▪ phase I, II, III and IV trials ▪ radiotherapy, radioimmunotherapy and radiosensitisers, microwaves, ultrasound, laser and phototherapy ▪ monitoring side effects
6.6 Psychological and behavioural	Application and evaluation of psychological and behavioural interventions in humans in clinical, community and applied settings ▪ phase I, II, III and IV trials ▪ cognitive behavioural therapy, electro-convulsive therapy, counselling, therapy and social interventions
6.7 Physical	Testing and evaluation of physical interventions in humans in a clinical, community or applied setting including

	▪ physical therapies, physiotherapy, occupational therapy, speech therapy, dietetics, osteopathy and exercise
6.8 Complementary	All aspects of testing, evaluation and provision of complementary approaches to conventional medicine in humans in a clinical, community or applied setting including ▪ hypnotherapy, massage, acupuncture and homeopathy ▪ issues relating to health and social services and health care delivery ▪ attitudes and beliefs of patients and health care professionals
6.9 Resources and infrastructure (evaluation of treatments)	▪ provision and distribution of resources related to clinical and applied therapeutic interventions ▪ infrastructure support for clinical and applied research networks and trials, consortia and centres

Research Activity Codes

7 Management of Diseases and Condition	Research into individual care needs and management of disease, conditions or ill health
7.1 Individual care needs	Studies of patients and service user care needs including - quality of life, management of acute and chronic symptoms, management of side effects, rehabilitation, long term morbidity and reproductive issues - psychological impact of illness - social and economic consequences of ill health - behaviour affecting disease management including secondary - prevention, compliance to treatment and attitudes and beliefs relating to seeking treatment - assessment of social care and health services needs - educational or communication interventions to promote self-care or improve health care by carers - impact on carers
7.2 End of life care	Studies involving all issues related to palliative care and end of life care including - assessment of patient, service user and carer needs - provision and evaluation of palliative and end of life care services - quality of life for patients and carers - evaluation of interventions for health and social care professionals - social, economic and policy issues - pain management for terminally ill people - bereavement
7.3 Management and decision making	conditions by health and social care professionals - attitudes, beliefs and behaviours of health and social care professionals - investigation of decision making including factors influencing diagnosis, treatment, referral and management strategies - educational interventions and communication practices - development of guidelines, interventions or models to assist decision making and management, including identifying symptoms, predicting outcomes and identifying individuals at risk - testing and evaluating management regimes and strategies
7.4 Resources and infrastructure (disease management)	development and/or distribution of resources and equipment for use by the community including informatics systems - infrastructure support for trials, networks, consortia and centres

Research Activity Codes

8 Health and Social Care Services Research	**Research into the provision and delivery of health and social care services, health policy and studies of research design, measurements and methodologies**
8.1 Organisation and delivery of services	Examining the organisation and provision of health and social care services and evaluating factors affecting the quality of care - workforce and career issues - organisation and management of services - access to health and social care and geographical variations in outcomes - effectiveness of different care settings and models of service delivery - evaluating quality of care including patient safety issues - evaluation of experiences of service users - assessment of current and future health care demands - development and evaluation of interventions to improve services
8.2 Health and welfare economics	Economic evaluation of health and social care interventions and delivery including - cost-benefit analysis of services including economic modelling - cost effectiveness or economic feasibility of implementing new interventions or technologies within health services - economic assessment of service productivity and outcomes - health care costs - development and evaluation of economic models of health care
8.3 Policy. ethics and research governance	- evaluation of local, regional and national healthcare policy - impact of legislation - synthesis and evaluation of evidence to inform policy - dissemination and implementation of research evidence - research ethics including use of personal data and biological material, consent and confidentiality - research governance and regulation processes including interpretation of guidelines - issues surrounding research subjects and donor recruitment
8.4 Research design and methodologies	Development of research designs and novel methodologies for health care including treatment, management and health services research - analytical innovation, methodological research, statistical methods and modelling - development of research measurements including outcome measures - development of methods of research assessment and evaluation - development and evaluation of research designs and methodologies
8.5 Resources and infrastructure (health services)	- development and distribution of resources for use by the community including informatics systems - infrastructure support for networks, trials, consortia and centres

STUDY DESIGN AND STATISTICAL CONSIDERATIONS * - CHECKLIST

All applicants must give careful thought to the following study design, methods and statistical considerations, and ensure that they are reflected in the grant application. Consider the following questions for the clinical research study design and methodological planning.

1. Is the main objective exploratory (for which a formal sample size justification is not relevant) or are you testing a quantitative hypothesis?
2. If the former, what are the population parameter/s you are trying to estimate? (E.g. annual incidence of AIDS, prevalence of teenage smokers, relative risk of a relapse etc)
3. If the latter, use the checklist below which could assist you to describe your study design and methods more clearly.
4. Some sample questions related to the check list below: (a) State the primary quantitative hypothesis (e.g. the hazard ratio is 0.5) and the required precision for the estimate in the form of a confidence interval e.g. 95% CI of the HR (0.3, 0.7)? (b) State the sample size required to achieve that precision. Be sure to specify the type 1 error, any other required assumptions needed and the sample size software / formula used in the calculation.

The following checklist provides guidelines for describing the study and design and methods as adapted from the CONSORT statement[4].

Area	Descriptor	Y/N/NA
METHODS Participants	Eligibility criteria for participants' description of settings/ locations where data are collected.	
Recruitment Methods	How will subjects be identified, enrolled and retained?	
Interventions	Detail the interventions intended for each group and how, when and by whom they are to be administered.	
Objectives hypotheses	Provide specific objectives or aims and related specific hypotheses.	
Outcomes	Clearly define primary and secondary outcome measures, AND when applicable, methods to enhance measurements quality (*e.g.*, multiple observations, assessor training).	
Sample size	How was sample size determined ? When applicable, explain any interim analyses and stopping rules.	
Randomization - Sequence generation	Method used to generate the random allocation sequence, and any restrictions (*e.g.*, blocking, stratification)	
Randomization - Allocation concealment	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone). Clarify whether the sequence will be concealed until interventions to be assigned.	
Randomization - Implementation	Who will generate the allocation sequence, who will enroll participants, and who will assign participants to their groups	
Blinding	How was blinding of the assigned treatment achieved for (i) subjects (ii) care-givers (iii) outcome assessors?	
Data collection	Outline how data will be collected, stored, managed. How will you ensure data quality (e.g. rater drift)?	
Adverse Events	How detected, measured, and managed?	
Study Period	When will enrollment start, stop, when is last data point?	
Statistical analyses for each hypothesis	What specific statistical analysis is planned for each primary and planned secondary hypothesis?	
Statistical Collaboration	Who provides design and statistical collaboration	

[4] The CONSORT is primarily for randomized controlled trials, but nevertheless has many features that would apply more generally to other types of clinical research projects. Visit http://www.consort-statement.org/index.aspx?o=1017 for more details.