# APPLICATION GUIDE

# CLINICAL TRIAL GRANT (CTG)


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## CLINICAL TRIAL GRANT (CTG)

### (A) Aim

1. The aim of the Clinical Trials Grant (CTG) is to enable clinicians to carry out clinical trials for the development of novel therapies, interventions and diagnostics, focusing on healthcare needs.

2. There are two schemes under the CTG:

   (I) CTG-Industry Collaborative Trials (CTG-ICT)
   (II) CTG-Investigator-Initiated Trials (CTG-IIT)

### (B) Eligibility Criteria

3. Each grant application must be led by a Clinical Principal Investigator (PI) who has to fulfil the following eligibility criteria listed below. Only one PI is allowed per application.

- Must fulfil HSA's requirements for PIs who are conducting clinical trials. PIs refer to HSA website for guidelines on conducting clinical trials. http://www.hsa.gov.sg/content/hsa/en/Health_Products_Regulation/Clinical_Trials/Overview/Introduction_to_Clinical_Trials.html (includes Investigator has to be a locally registered doctor or dentist and is a senior doctor/specialist in his/her field of practice).

- PI must be clinically qualified (i.e. with MD/MBBS/BDS) and preferably with post-graduate clinical training and experience.

- PI to hold a primary appointment in a local public hospitals/public health institutions/national specialty centres/public universities/Academic Medical Centres and salaried by the institution.

- Be 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) or substantial publication record.

- Have a laboratory or clinical research program that carries out research in Singapore.

- Hold a minimum of 9 months employment with a local Singapore institution, and fulfilling full time residency in Singapore over a period of the calendar year.

- No outstanding reports from previous NRF, BMRC, NMRC grants and other national grants.

### (C) CTG Schemes – Description, Funding quantum and duration, Grant call frequency, Submission and Deadline

#### *(I) CTG-Industry Collaborative Trials (CTG-ICT) scheme*

**Description**

4. This scheme supports ICTs that involve both clinician and company contributing intellectual inputs and funds to conduct the trial and developing novel or pre-existing therapies/drugs/medical device for new indications.

5. **This scheme does not support trials that are fully funded/sponsored by companies.** Such trials typically do not require the clinicians' intellectual inputs as the clinical trial protocol has already been designed by the company, and the clinicians' involvement is more for subject/patient recruitment.

6. From 1 Nov 2019 onwards: Pls note that CTG-ICT will have a focus on early phase trials.

**Prerequisites**

7. The prerequisite for application is PI's ability to obtain industry contribution of at least 70% (cash or in-kind) of the Total Project Costs (TPC). The TPC and industry contribution will be based on the Research Collaborative Agreement (RCA) between the host institution (HI) and the industry partner.

8. In IGMS, pls ensure that:

   (i) the industry contribution is clearly indicated in Section 3 of the proposal in the application form and

   (ii) the RCA is uploaded in the "Other Attachments" section/tab. The RCA should clearly indicate the budget information (PI and industry contribution, and the TPC as reflected in the proposal).

9. Pls note that:
   (i) the admissible in-kind drug cost contribution from the industry partner is limited to equivalent to the non-drug cost contribution (pls refer to slide 16 of NMRC May 2018 Grant Call Roadshow slides for an example of the calculation). http://www.nmrc.gov.sg/content/dam/nmrc_internet/nmrc2.0/roadShows/NMRC%20May%202018%20Grant%20Call%20Roadshow%20Slides.pdf

   (ii) If the project is awarded, the PI/HI will be required to:
   - ensure that the industry contribution is met at the completion of the awarded project
   - submit yearly reporting on the industry contribution (Refer to the "Guidelines for Annual Reporting of Industry Contributions" to complete "Industry Contribution Form" with supporting documents e.g. receipts, invoices), together with the annual progress report.

(Pls see the 2 files "Industry Contribution Form" and "Guidelines for the Annual Reporting of Industry Contributions" in "IGMS Application Templates_CTG" folder)

**Funding Quantum and duration**

10. The scheme will cover up to 30% of the TPC (inclusive of 20% indirect costs).

11. Funding for each project is open and for a period of up to 5 years.

**Review Process**

12. All applications will undergo a streamlined review process and the assessment criteria include the following:

- Scientific and clinical merit of proposal
- Track record of applicants
- Focus on HBMS 5 priority therapeutic areas and early phase trials (1 Nov 2019 onwards)
- Address unmet clinical need in SG with good potential to be implemented in local healthcare system
- Agreement with industry partner on IP
- Result in technology transfer, talent and/or capability building which SG would like to gain (or strengthen SG's position in points 3 and 4)
- Lead to some form of return on investment for SG e.g. healthcare savings, discounted price for use of therapy, royalties, further contribution to research activities etc)

13. The review process will take about 2 months after application endorsement by HI.

**Grant Call Frequency**

14. This scheme is open for application throughout the year, i.e. no formal grant calls will be held. Applicants can submit their proposals via IGMS at any time.

**Submission and Deadline**

15. **In the CTG-ICT scheme, PI will submit a Letter of Intent (LOI) application. Pls complete all sections of the online application form in the IGMS, and sections in the proposal template which are highlighted in blue colour.**

**If the application is shortlisted, the PI will then be required to complete and submit the rest of the sections in the proposal template.**

16. Applicants can submit their proposals at any time. It is **mandatory** for all applications to be submitted and endorsed by the HI's Director of Research (DOR) via IGMS. Internal Host Institution submission deadline may apply, please check with your Research Office for more information.

### *(II) CTG-Investigator Initiated Trials (CTG-IIT) scheme*

**Description**

17. This scheme will support IITs of both early and late phase which are initiated and driven by clinicians who are interested to conduct trials on novel or pre-existing drugs/medical device/interventions for new indications.

18. No minimum company contribution, however, applications with industry contribution would have higher priority.

19. For applications with industry contribution, in IGMS, pls ensure that:

(i) the industry contribution is clearly indicated in Section 3 of the proposal in the application form and

(ii) the RCA or other supporting documents indicating the industry contribution are uploaded in the "Other Attachments" section/tab. The RCA should clearly indicate the budget information (PI and industry contribution, and the TPC as reflected in the proposal).

(iii) Pls note that if the project is awarded, the PI/HI will be required to:
- ensure that the industry contribution is met at the completion of the awarded project
- submit yearly reporting on the industry contribution (Refer to the "Guidelines for Annual Reporting of Industry Contributions" to complete "Industry Contribution Form" with supporting documents e.g. receipts, invoices), together with the annual progress report.

(Pls see the 2 files "Industry Contribution Form" and "Guidelines for the Annual Reporting of Industry Contributions" in "Other Attachments" Template folder)

**Funding Quantum and duration**

20. CTG-IIT is funded by NRF Central Gap.

21. Funding for each project is capped at $1.5mil **(without overheads/indirect cost)**. Please refer to the NRF Central Gap Fund guidelines for more details. https://www.nrf.gov.sg/docs/default-source/default-document-library/central-gap-fund-application-guidelines-v2.pdf.

22. Funding duration is up to 3 years. Projects with duration of more than 3 years will be evaluated on a case-by-case basis.

**Review Process**

23. All applications will be evaluated through a two stage review process comprising a peer review stage followed by a Local Review Panel (LRP). The assessment criteria include the following:
    - Scientific and clinical merit of proposal
    - Track record of applicants
    - Focus on HBMS 5 priority therapeutic areas
    - Address unmet clinical need in SG with good potential to be implemented in local healthcare system, and commitment from HI to implement if the IIT results are promising
    - Involve local IPs and formation of businesses
    - Lead to some form of return on investment for SG e.g. healthcare savings, discounted price for use of therapy, royalties, further contribution to research activities etc)

24. The review process will take about 6 months after application endorsement by HI.

**Grant Call Frequency**

25. Proposals are to be submitted via IGMS in response to formal NMRC CTG-IIT grant calls in May and in Nov.

**Submission and Deadline**

26. **In the CTG-IIT scheme, applications are to be accompanied with:**
    **a) A letter of support from the HI and also from the PI's Head of Department to show their commitment to adopt the IIT outcome**

    **b) In-kind support from the HI (could include EOM, equipment and OOE support from grants received by the HI e.g. NMRC Centre Grant, Clinical Research Coordinator Funding Award, or internal funds)**

    - **Pls address both documents to "NMRC" (pls do not address to staff or review panel)**

27. It is **mandatory** for all applications to be submitted and endorsed by HI's DOR via IGMS by **29 Nov 2019, 5pm**.

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

29. Please ensure that all online submissions are endorsed by the corresponding HI's DOR by the closing date. We will not entertain any late submissions or submissions from individual applicants without endorsement from the HI's DOR.

## (D) Research Themes

30. The CTG is open to application on all research themes. However, there will be strategic consideration for applications which focus on the following priority areas:

    - Cancers
    - Cardiovascular diseases
    - Diabetes mellitus and other metabolic/ endocrine disorders
    - Infectious diseases
    - Neurological and sense disorders

## (E) Reporting requirements

31. CTG-ICT and CTG-IIT grantees (for CTG-IIT grantees prior to May 2018 grant call) are required to provide an annual report to NMRC and to submit a final report to NMRC within 3 months from the project completion date.

32. From May 2018 grant call onwards, CTG-IIT is funded by NRF Central Gap. Grantees are required to provide bi-annual report to NMRC. Please refer to the NRF Central Gap Fund guidelines for more details. https://www.nrf.gov.sg/docs/default-source/default-document-library/central-gap-fund-application-guidelines-v2.pdf.

## (F) Enquiries

33. For further enquiries, you may contact Dr Sharon Ling at Sharon_Ling@moh.gov.sg.

## GENERAL INSTRUCTIONS

1. Please prepare your application **using the templates available on the IGMS** and upload the completed documents to the relevant sections in IGMS:
   (i) Research Proposal
   (ii) CVs (PI, Co-I/Collab)
   (iii) Research Team Signatures and Other Supporting Details
   (iv) Supporting Documents for CTG-ICT and CTG-IIT applications

2. Any softcopy document must be uploaded to IGMS in Word Document or PDF format (please do not submit scanned PDF format except for signatures). Please adhere to the number of pages where specified and reformat softcopies such that all blank or irrelevant pages are removed.

3. The applicants are required to complete the grant submission using the IGMS online submission system.

4. Once you have completed your application in IGMS, please proceed to download a copy for your safekeeping (please refer to IGMS user guide for instructions).

5. **Resubmission attempts are capped at two times. Funding is not guaranteed for resubmitted proposal.** (Resubmission refers to proposals resubmitted based on LRP/ 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).

6. In any single grant call, each PI is allowed to submit up to one application per grant type.

7. There is no limit to the number of Co-Investigators (Co-Is)[1] or Collaborators[2]. **Please specify and describe clearly the roles of Co-Investigators and Collaborators in the relevant section.**

8. **Note that Co-Investigators need to hold at least an adjunct position in a local public institution.** Researchers from overseas institutions or private companies can only participate as collaborators. The terms of collaboration with overseas research institutions and private companies must conform to NMRC's existing policies.

9. PI's CV is limited to 2 pages. Co-Investigators' and Collaborators' CVs are limited to 1 page each. Please indicate NA if the required information is not applicable. Please take note that NMRC will not be responsible for any missing information not provided in the CV.

10. Use **Arial font size 10** for all attachment/text.

11. 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.

12. Refer to Appendix 1 for details on Health Research Classification System (HRCS) to complete "Field of Research" in nGager.

13. Refer to Appendix 2 for checklist on Study Design and Statistical Considerations to complete "Methods/Approach" section in the research proposal.

## Submission of Applications

- It is mandatory for all applications to be submitted and endorsed by Host Institution's Director of Research (DOR) online via IGMS **by 29 November 2019, 5pm**. Internal Host Institution submission

[1] **Definition of 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 as compared to a collaborator and is considered a key personnel.

[2] **Definition of Collaborator**: An individual involved in the scientific development and execution of project. A collaborator would typically devote a specific percent of effort to the project.

deadlines may apply, please check with your Office of Research (ORE) for more information. We will not entertain any late submissions or submissions from individual applicants without endorsement from the Host Institution. Please note that any clarifications sought by the DOR/ORE will need to be addressed by the PI prior to submission **by 29 November 2019, 5pm**.

- Please note that NMRC will reject application upon submission if:
  - Any of the required documents was not submitted (Please refer to Read-Me file for the list of required documents)
  - Wrong template (e.g., outdated, different programme's) was used for any of the required documents (Please use latest templates as available in IGMS)
  - Any of the Proposal or CV documents exceeds page limits

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

## Additional Document required for Re-submission Applications

- Resubmission refers to proposals resubmitted based on LRP / 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

- A proposal can only be resubmitted **two times**. Proposal which has been resubmitted for more than two times will be rejected.

- Append the following documents to the end of the application as Annexes:

  - A document itemizing how the revised proposal (i.e. re-submission application) has addressed past reviewers'/panel's comments and highlight new features or merits of the revised proposal (**Annex B**)
  - International Reviewers' reports of previous unsuccessful application (as images inserted in the Annex document); Rebuttal to the international reviewers; Local Reviewers' reports (as images inserted in the Annex document), where applicable; Response to local reviewers (where applicable); Panel's comments (where applicable); and Response to the panel (where applicable) (in the above order as **Annex C**)

## Additional Document required for Renewal Applications (Follow up study from NMRC projects)

- Submit a progress/final report of the existing project to indicate the progress and outputs of the project in the prescribed NMRC reporting format (i.e. progress/ final report) as **Annex D.**

- As this section may be submitted to both overseas and local reviewers, PI is to ensure that all sensitive information on IP issues and such are cleared from the Host Institution before submitting to NMRC.

**Appendix 1**

# 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<br>- genes and gene products<br>- molecular, cellular and physiological structures and function<br>- biological pathways and processes including normal immune function<br>- developmental studies and normal ageing<br>- bioinformatics and structural studies<br>- 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<br>- perception, cognition and learning processes<br>- social and cultural beliefs<br>- individual or group characteristics and behaviours<br>- politics, economies and urban development<br>- 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<br>- bioengineering and biophysics<br>- chemical structures, interactions and properties<br>- molecular modelling<br>- material science |
| 1.4 Methodologies and measurement | Development of novel underpinning research measures and analytical methodologies including<br>- development of statistical methods and algorithms for genomic analysis<br>- development of mapping methodologies and novel data comparison methods<br>- 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<br>- 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<br>- genes and gene products, molecular, cellular and physiological structures and functions<br>- biological factors linked to ethnicity, age, gender, pregnancy and body weight<br>- endogenous biological factors or pathways involved in responses to infection or damage by external factors<br>- metastases, degenerative processes, regeneration and repair<br>- complications, reoccurrence and secondary conditions<br>- bioinformatics and structural studies<br>- 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<br>- physical agents, occupational hazards, environmental surroundings, radiation and pollution<br>- chemicals and nutrients<br>- 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<br>- individual or group behaviours and lifestyle<br>- cultural or religious beliefs or practices<br>- ethnicity, age and gender differences<br>- 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<br>- methodological innovation and modelling complex epidemiological data<br>- development and evaluation of novel research designs<br>- development of epidemiological research measurements includingoutcome measures<br>- 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<br>- 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<br>- risk behaviours associated with diet, tobacco use, physical activity, alcohol consumption, sexual health and substance misuse<br>- age, gender, cultural or religious practices<br>- public health policy, health communication and educational interventions<br>- 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<br>- radiation, second-hand smoke, physical and chemical agents,<br>- occupational hazards and environmental surroundings<br>- contraceptive devices<br>- infectious agents<br>- policy, educational and physical interventions |
| 3.3 Nutrition and chemoprevention | Research on chemopreventative agents and health protective effects of nutrients including<br>- development, characterisation and mechanism of action<br>- chemical contraceptives<br>- testing and evaluation in model systems and clinical, applied and community settings<br>- evaluation of evidence to inform policy |
| 3.4 Vaccines | Research on vaccines for prevention of disease including<br>- discovery, development and testing of vaccines and vaccination in model systems<br>- mechanism of action<br>- development, implementation and evaluation of vaccination programmes and studies to increase uptake<br>- 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<br>- 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<br>- biological and psychological markers<br>- diagnostic and monitoring devices, imaging, scanning, predictive and<br>- diagnostic tests<br>- development and characterisation of models<br>- 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<br>- assessment of sensitivity, efficacy, specificity. predictive and prognostic value, reproducibility and safety<br>- medical devices, imaging, diagnostic and predictive tests<br>- 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<br>- attitudes and beliefs including cultural and religious practices<br>- issues relating to gender, age and ethnicity<br>- genetic counselling and decision making<br>- psychological, social and economic factors<br>- development, implementation and evaluation of interventions to promote screening including policy, education and communication |
| 4.4 Population screening | Studies investigating population screening programmes including<br>- feasibility studies, pilot studies and trials<br>- evaluation of effectiveness, benefits and economic evaluation<br>- impact on health services and policy issues<br>- 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<br>- 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<br>- drug screening and development of delivery systems<br>- mechanism of action including side effects and drug resistance<br>- pharmacogenetics, prediction of genetic variation and responses to drugs<br>- 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<br>- gene therapy, stem cells therapy, in vitro fertilisation and tissue engineering<br>- development of delivery systems<br>- development of culture systems<br>- testing in in vitro and in vivo model systems |
| 5.3 Medical devices | Discovery and development of medical devices including<br>- implantable devices, mobility aids, dressings, medical equipment and prostheses<br>- biological safety assessments and investigation of adverse events<br>- sterilisation and decontamination of equipment or surfaces<br>- testing in in vitro and in vivo model systems |
| 5.4 Surgery | Development of surgical, obstetric and dental interventions including<br>- histocompatability, transfusions, transplantations including xenograft studies and bone marrow transplants<br>- mechanisms of recovery, tolerance, rejection and side effects including infection<br>- testing in in vitro and in vivo model systems |
| 5.5 Radiotherapy | Discovery and development of interventions including<br>- radiobiology, radiotherapy, radioimmunotherapy, radiosensitisers, microwaves, ultrasound, laser and phototherapy<br>- development of delivery systems<br>- investigation of mechanisms of action and side effects<br>- testing in in vitro and in vivo model systems |
| 5.6 Psychological and behavioural | Development of psychological and behavioural interventions including<br>- cognitive behavioural therapy, electro-convulsive therapy, counselling, therapy and social interventions<br>- testing in model systems |
| 5.7 Physical | Development of physical interventions including<br>- physical therapies, physiotherapy, occupational therapy, speech therapy, dietetics, exercise and osteopathy<br>- mechanisms of action<br>- testing in model systems |
| 5.8 Complementary | Discovery and development of complementary approaches to conventional medical therapies including<br>- hypnotherapy, meditation, massage, acupuncture and homeopathy<br>- mechanisms of action<br>- 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<br>↓ 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<br>↓ small scale settings and pilot studies<br>↓ phase I, II, III and IV trials<br>↓ assessing sensitivity, efficacy, specificity, relapse, survival, therapeutic value, pharmacokinetics, reproducibility and safety<br>↓ 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<br>↓ small scale and pilot studies<br>↓ phase I, II, III and IV trials<br>↓ gene therapy, stem cell therapy, in vitro fertilisation, tissue engineering<br>↓ 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<br>↓ implantable devices, mobility aids, dressings, medical equipment and prostheses<br>↓ 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<br>↓ small scale and pilot studies<br>↓ phase I, II, III and IV trials<br>↓ procedures including organ and bone marrow transplantation, tissue grafts and transfusions<br>↓ monitoring outcomes, side effects and rejection |
| 6.5 Radiotherapy | Clinical application and evaluation of interventions in humans including<br>↓ small scale and pilot studies<br>↓ phase I, II, III and IV trials<br>↓ radiotherapy, radioimmunotherapy and radiosensitisers, microwaves, ultrasound, laser and phototherapy<br>↓ monitoring side effects |
| 6.6 Psychological and behavioural | Application and evaluation of psychological and behavioural interventions<br>in humans in clinical, community and applied settings<br>↓ phase I, II, III and IV trials<br>↓ 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<br>↓ 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<br>- hypnotherapy, massage, acupuncture and homeopathy<br>- issues relating to health and social services and health care delivery<br>- 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<br>- 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<br>- quality of life, management of acute and chronic symptoms, management of side effects, rehabilitation, long term morbidity and reproductive issues<br>- psychological impact of illness<br>- social and economic consequences of ill health<br>- behaviour affecting disease management including secondary<br>- prevention, compliance to treatment and attitudes and beliefs relating to seeking treatment<br>- assessment of social care and health services needs<br>- educational or communication interventions to promote self-care or improve health care by carers<br>- impact on carers |
| 7.2 End of life care | Studies involving all issues related to palliative care and end of life care including<br>- assessment of patient, service user and carer needs<br>- provision and evaluation of palliative and end of life care services<br>- quality of life for patients and carers<br>- evaluation of interventions for health and social care professionals<br>- social, economic and policy issues<br>- pain management for terminally ill people<br>- bereavement |
| 7.3 Management and decision making | conditions by health and social care professionals<br>- attitudes, beliefs and behaviours of health and social care professionals<br>- investigation of decision making including factors influencing diagnosis, treatment, referral and management strategies<br>- educational interventions and communication practices<br>- development of guidelines, interventions or models to assist decision making and management, including identifying symptoms, predicting outcomes and identifying individuals at risk<br>- 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<br>- 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<br>- workforce and career issues<br>- organisation and management of services<br>- access to health and social care and geographical variations in outcomes<br>- effectiveness of different care settings and models of service delivery<br>- evaluating quality of care including patient safety issues<br>- evaluation of experiences of service users<br>- assessment of current and future health care demands<br>- 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<br>- cost-benefit analysis of services including economic modelling<br>- cost effectiveness or economic feasibility of implementing new interventions or technologies within health services<br>- economic assessment of service productivity and outcomes<br>- health care costs<br>- development and evaluation of economic models of health care |
| 8.3 Policy. ethics and research governance | - evaluation of local, regional and national healthcare policy<br>- impact of legislation<br>- synthesis and evaluation of evidence to inform policy<br>- dissemination and implementation of research evidence<br>- research ethics including use of personal data and biological material, consent and confidentiality<br>- research governance and regulation processes including interpretation of guidelines<br>- 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<br>- analytical innovation, methodological research, statistical methods and modelling<br>- development of research measurements including outcome measures<br>- development of methods of research assessment and evaluation<br>- 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<br>- infrastructure support for networks, trials, consortia and centres |

**Appendix 2**

## *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[3].

| 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. | |

[3] 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.

| | | |
|---|---|---|
| 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 | |