Efficacy and Mechanism Evaluation Programme

Call for proposals into mechanisms of action of health interventions

Closing date: 1:00 pm, 20th November 2018 (one stage straight to stage 2 application)

The EME Programme invites proposals for hypothesis driven research into the underlying mechanisms of action of clinical and public health interventions. Studies must utilise patients or samples from identifiable cohorts from current or completed NIHR-funded projects from the following programmes: i4i, EME (including the MRC/NIHR transferred portfolio), HS&DR, HTA, PHR, RfPB and PGfAR.

Proposals will be accepted across a wide range of interventions; including behavioural, pharmaceutical, psychological, surgical and public health interventions. The research should be hypothesis driven, relevant to the intervention and outcomes proposed by the original study and add significantly to the scientific understanding of the mechanisms of action of the intervention.

The proposed research may involve the analysis or reanalysis of previously stored specimens or data, or the collection of new specimens or new data for additional analysis, provided it is obtained from the study participants. Applicants must have agreement from the CI of the original NIHR study.

Discovery of new biomarkers is not within the remit of the EME Programme.

Applicants will need to make a strong case for how a better understanding of the mechanisms of action will potentially contribute to the future use or development of the technology, future wealth creation and for the ultimate benefit of individual patients' or the wider NHS.

Important Information for Applicants to this call

Programme remit

The EME Programme funds ambitious studies evaluating interventions that have the potential to make a step-change in the promotion of health, treatment of disease and improvement of rehabilitation or long-term care. Within these studies EME supports research to improve the understanding of the mechanisms of both diseases and treatments.

The programme supports translational research evaluating a wide range of novel or re-purposed interventions. The interventions may include diagnostic or prognostic tests and decision-making tools, drugs or biological compounds, psychological treatments, medical devices, and public health initiatives delivered within the NHS.

The EME Programme is funded by the MRC and NIHR, with contributions from the CSO in Scotland, Health and Care Research in Wales and the HSC R&D Division, Public Health Agency in Northern Ireland. It is managed by the NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC) based at the University of Southampton.

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The EME Programme primarily supports clinical trials, and other robustly designed studies that test the efficacy of interventions. The interventions should have the potential to improve patient care or benefit the public. The programme will only support studies where there is sufficient evidence that the intervention might work in man, i.e. that there is 'proof of concept (pdf, 55.19 KB) '.

Innovative study designs involving stratification, the use of routinely collected digital data or novel methodologies are strongly encouraged.

Where appropriate, the programme encourages hypothesis-testing mechanistic studies (pdf, 124.55 KB) integrated within the main efficacy study. These studies could explore the mechanisms of action of the intervention, the causes of differing responses, or promote an understanding of any potential adverse effects and how these could be reduced; they could also contribute to understanding of the disease. The programme will also support mechanistic studies that follow on from on-going or completed clinical studies funded by the NIHR which can use data or samples from these studies.

The programme will accept applications for studies that use clinical or well-validated surrogate outcomes. It will also consider studies that validate potential surrogate outcomes against a primary clinical outcome, within the main clinical trial.

The EME programme WILL support:

- Research to determine proof of clinical efficacy, size of effect, and long-term safety in a well-defined population.
- The evaluation of a broad range of interventions that have the potential to maintain health, treat disease or improve recovery.
- Hypothesis-testing research based on an efficacy study, to explore the mechanisms of action of interventions, causes of differing responses or disease mechanisms. These studies use data or samples obtained and stored from both treatment and control groups of a clinical study, to arrive at conclusions that would not arise from a simple cohort study.
- Proposals that include a series of linked stages (usually 2 to 3) with progression to the main clinical evaluation dependent on the outcome of the previous stage(s). The criteria for progression must be clearly defined. The main clinical evaluation should require more than 75% of the total project costs and commence within 18 months of the project start date.
- Pilot and feasibility studies where the main study would be within the remit of the EME programme. These studies may be either stand-alone or can be the initial part of a staged project that includes the main clinical evaluation as a subsequent stage.
- The limited steps needed to progress the development of an intervention to a stage suitable for use in an accredited clinical service when included as an initial stage prior to commencing the main clinical evaluation.
- Studies using novel or infrequently-used study designs that increase the value of a study, by maximising the chances of demonstrating the benefit of an intervention, increasing the knowledge that can be gained through the study, or by making the study more efficient.

The EME Programme WILL NOT support:

- Large effectiveness studies that test the impact of the introduction of an intervention in the wider NHS.
- Hypothesis-generating studies based on sample or data collections from patient cohorts.
- Confirmatory studies, equivalence studies, 'confidence in effect' studies or studies of incremental modifications to existing interventions.
- Research into areas where the health need is primarily outside the UK.
- Any research involving animals or animal tissues (see the NIHR research page for more information).

Applicant eligibility

Researchers in England, Northern Ireland, Scotland and Wales are eligible to apply for funding under this Programme. Anyone who considers that they can carry out high-quality research is likely to be eligible. If you have any concerns regarding your eligibility to apply we advise that you contact us before completing an application. We welcome applications from all sectors.

Studies funded by the EME Programme are generally UK based. We will consider funding an international study where the chief investigator and lead institution are based in the UK and the study is relevant to and a priority for the UK population, and where overseas recruitment is funded from other sources. It will be exceptional for NIHR programmes to fund recruitment overseas. The EME Programme is open to bids to support a UK recruitment arm of an international study where the study is relevant to and a priority for the UK population; a UK based principal investigator should be the lead applicant. Each project will be considered on a case by case basis and applicants interested in submitting a proposal for an international study should contact us for advice.

Collaboration and team expertise

Proposals should involve a multi-disciplinary team with appropriate skills and experience, including an appropriately experienced statistician on the study team. The involvement of an accredited Clinical Trials Unit (CTU) is strongly encouraged in the design of clinical trials. Where appropriate, applicants are expected to work with suitably accredited clinical research facilities.

Applications to this call should be in the form of a collaboration. All applications should include significant contributions from at least two of the following partners; industry, academia, and the NHS. The EME Programme is particularly keen to encourage collaboration with small and medium enterprises. The involvement of charities is also welcome. Evidence of this collaboration must be provided and a draft collaboration agreement will be required at the full proposal stage.

The EME Programme welcomes applications proposing joint funding arrangements. You must clearly demonstrate how the arrangement would work in practice and be explicit about where responsibility lies contractually in terms of publication, and research governance issues for example. We expect that any other organisations contributing funding would provide an ‘open grant' and not require any terms, conditions or limitations on the research. The Programme would require assurance that the funding contribution would be guaranteed for the duration of the research, and a letter of intent should be included with the application. If your application is

successful, you should note that the EME Programme will require sight of the agreement between you and any other funding partners before any contract is issued.

Where your research proposal involves industry collaboration, you should ensure that the arrangements and details are determined early in the study development. The EME Programme will require assurance that any industry collaboration allows transparency in the project design and in the analysis and publication of results (including if these are negative). If the collaboration involves the supply of reagents, drugs or other technologies, we will require written assurances that the industry collaborator will provide these products for the duration of the study.

Timescales and funding

There are no fixed limits on the duration of projects and proposals should be tailored to fully address the questions posed. Applicants should be aware that they are competing for limited funds and proposals should represent good value for money. All funding requested should be clearly justified, but there is no upper limit.

Public Involvement

The EME Programme expects patient and public involvement in study design, implementation and dissemination of results. Applications must demonstrate how patients or members of the public have been involved in the study design and how they will be involved in the conduct and management of the trial. Patient, public or carer representation is required on management and steering committees. Comments from public and patient reviewers will be obtained during peer review and at the EME Board. For further guidance please see the EME website.

Project Management and monitoring of studies

Where appropriate, projects funded through this call should be organised into distinct stages (usually up to three). At the end of each stage there should be clearly delineated go/no-go decision points with measurable criteria which will allow an assessment of whether the stage has completed successfully. The purpose of this delineation is to clearly identify critical points that determine whether the research should proceed to the next stage. It is anticipated that there will be a significant number of projects that will fail to meet criteria in the early stages. The EME Programme retains the right to reassess project progress in light of other new developments in the research area before subsequent stages of funding are released.

Within each stage it is expected that there will be a number of milestones which will allow the project team and EME Programme to track progress through routine project reporting. Applicants will need to demonstrate a clear management plan for all stages of the project as well as detailed plans for how they will actively manage individual stages.

Research Networks

The EME Programme expects that applicants will work, where appropriate, with the relevant NIHR Clinical Research Network.

Governance and Regulation

Applicants should follow the Medical Research Council's Good Clinical Practice guidelines in planning how studies, particularly RCTs, will be supervised.

Note that trials involving medicinal products must comply with 'The Medicines for Human Use (Clinical Trials) Regulations 2004'. In the case of such trials, the NIHR expects the employing institution of the chief investigator to be nominated as the sponsor. Other institutions may wish to take on this responsibility or agree co-sponsorship with the employing institution. The NIHR is prepared to accept the nomination of multiple sponsors. Applicants who are asked to submit a full proposal will need to obtain confirmation of a sponsor(s) to complete their application. The NIHR reserves the right to withdraw from funding the project if they are not satisfied with the arrangements put in place to conduct the trial.

The MHRA (info@mhra.gsi.gov.uk) can provide guidance as to whether your trial would be covered by the regulations. The Department of Health/MRC website also contains the latest information about Clinical Trials regulations and a helpful FAQ page.

Application Assessment Process and Criteria for Assessment

For information about the Application Assessment Process and Criteria for Assessment, please see https://www.nihr.ac.uk/eme

Additional Resources for Applicants

For additional resources to support the development of your applications, please see https://www.nihr.ac.uk/eme

Making an application

If you wish to submit an outline proposal please complete the web based application form.

Further Information

The EME team welcomes enquiries at eme@nihr.ac.uk or 02380 594303.

In line with the government's transparency agenda, any contract resulting from this tender may be published in its entirety to the general public.