

Efficacy and Mechanism Evaluation Programme

Call for research proposals (17/60 Researcher- Led)

Closing date: 1:00 pm, 28th November 2017 (two stage – outline to full)

Detailed call specification

Applications are sought for research into interventions that are based or used by the NHS and its partners. This document provides the detailed call specification for applications to the EME researcher-led workstream. Applicants should note:

- applications should focus on establishing efficacy of an intervention;
- proof of concept in humans for the intervention already needs to be established and should be clearly demonstrated in the application;
- applications may include embedded mechanistic evaluations, however, stand-alone mechanistic studies are excluded from this call;
- applications may investigate novel or repurposed interventions and tests;
- the discovery of new biomarkers is excluded from this call;
- studies involving incremental or minor improvements to existing technologies are excluded from this call.

Applications are expected to set out programmes of work which may contain distinct stages. It is expected that the early stages of the study will, if successful, lead onto a full evaluative clinical study or trial, which is in the remit of the EME Programme. This study must also be included and clearly specified within the application. Clinical trials embedded within the programme of work must be large enough to detect a meaningful effect.

Applications to this call may also include initial stages such as:

- The limited steps needed to progress the development of an intervention to a stage suitable for use in an accredited clinical service;
- Prospective clinical work or retrospective research utilising existing clinical samples or data to inform the main study;
- Pilot or feasibility studies.

As a rough guide it is expected that these early stages will be complete within the first 18 months of the project and must not contribute more than 25% to the total cost or duration of the project.

Applicants will need to make a strong case for the future importance of the intervention through providing a measurable positive impact on health, innovation or future wealth creation and for the ultimate benefit of individual patients' or the wider NHS.

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 repurposed 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 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'.

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 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 welcomes studies adopting novel and efficient study designs or that include the development or testing of new methodologies in an embedded methodological study (EMS). Where delivery of the EMS is integral to the main efficacy trial the additional costs should be modest and the purpose should be to explore issues that may potentially increase the efficiency of trials and value for money. The proposed work should be included in the EME application. Where the EMS requires more substantial funding and can be delivered independently from the running of the main trial, then applicants might wish to consider applying to the MRC-NIHR Methodology Research Programme (MRP). <http://www.mrc.ac.uk/funding/browse/methodology-research-programme/> Any such

application would be independent of the application to the EME Programme. For more information please contact the MRP programme: MRPGrants@headoffice.mrc.ac.uk

The NIHR programmes and research funding schemes have a highlight notice for Complex Health and Care Needs in Older People. This highlight notice indicates the continuing interest of NIHR in receiving research proposals in this area, and particularly those addressing Frailty; Transitions in care, service delivery and models of care; Medicines management/polypharmacy; Promoting healthy ageing/preventing ill health; Patient-centred decision making.

For details of this highlight notice, please see <https://www.nihr.ac.uk/themedcalls>. Please note that the EME researcher led call is open to all relevant research areas, and does not just include this highlight notice. If you are responding to the highlight notice, please indicate this in the application form in Section 6, Question 1 'What is the problem being addressed?'

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).

Guidance on Applications

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 and recommend that lead applicants from Industry contact the EME office prior to submitting an application.

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.

The EME Programme is funded by the MRC and NIHR, with contributions from the CSO in Scotland and NISCHR 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.

Collaboration and team expertise

The EME researcher-led workstream welcomes applications proposing joint funding arrangements or collaboration with other organisations. The EME Board requires you to clearly explain how the arrangement would work in practice and to be explicit about where responsibility lies contractually in

terms of publication, and research governance issues. The EME researcher-led workstream will support studies involving partnerships with industry where these are for public benefit, and are not for the exclusive benefit of the industry partner. Where your research proposal involves industry collaboration, you should ensure the arrangements and details are determined early in the study development, and a draft collaboration agreement must be provided at the full proposal stage.

Proposals should demonstrate 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.

It is acceptable to have applicants from outside the UK and EME research may be conducted outside the UK where this is the best means of meeting a research requirement relevant to healthcare in the UK. The rationale for such an application should be clearly set out and each case will be judged on its merits.

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.

Project Management and monitoring of studies

Projects funded through the EME researcher-led workstream will be expected to provide detailed project timetable including milestones to represent specific steps towards achieving the stated research objectives. Milestones should include a defined start and end date, be measurable, concise and realistic as they will be used for project monitoring purposes. The precise type and number of milestones will depend on the size and nature of the project. If your application is successful, you will be required to submit progress reports against which relevant milestones will be checked. These progress reports will be based on the project timetable and milestones, and will occur at approximately six month intervals.

Public Involvement

The EME Programme expects Patient and public involvement (PPI) 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 a trial. Patient/public/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](#).

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 \(info@mhra.gsi.gov.uk\)](mailto: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.