21/609 Efficacy and Mechanism Evaluation Programme researcher-led

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Medical Research Council NIHR | National Institute for Health Research

Contents

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.

Applications are sought for research into the efficacy and/or mechanism of interventions that are based in or used by the NHS and its partners. This document provides the detailed call specification for applications to the EME researcher-led workstream, which includes:

- **Efficacy studies**

  These aim to evaluate the efficacy of a wide range of interventions, where there is some human 'proof-of-concept', i.e. a signal that the technology may work.

- **Mechanistic studies**

  These aim to test hypotheses around the mechanism of action of an intervention, making use of patients, data

or samples from other studies.

- **Combined Efficacy and Mechanistic studies**, which both evaluate a intervention and test hypotheses around its mechanism of action within the same study.

Important information for applicants

Efficacy studies

The EME Programme supports translational research evaluating a wide range of novel or repurposed interventions and technologies. These may include but are not limited to diagnostic or prognostic tests and decision-making tools, drugs or biological compounds, behavioural therapies, medical devices, and public health initiatives delivered within the NHS.

EME 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'. Where appropriate, the programme encourages hypothesis-testing mechanistic studies integrated within the main efficacy study, but this is not a requirement.

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

Applications may set out programmes of work which 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 big data or clinical samples 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. Applicants should read the details of the EME remit.

Mechanistic studies

Mechanistic studies may be submitted as standalone applications or can form part of an application to EME to conduct an efficacy study. Mechanistic proposals will be accepted across a wide range of interventions; including behavioural, pharmaceutical, psychological, surgical and public health interventions. The research should be hypothesis-testing, 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. Funding **will not** be available for hypothesis-generating studies.

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

Standalone mechanistic studies must utilise patients and data or samples from identifiable cohorts and **must not** involve recruitment of new patients. 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. These must be from:

- Current or completed NIHR-funded projects from the following programmes: i4i, EME (including the MRC/NIHR transferred portfolio), HSDR, HTA, PHR, RfPB and PGfAR or equivalent funding from the Devolved Administrations. If applicable, please also consider whether this research needs to run concurrently with the main trial, rather than after results have been reported

OR

- Non-NIHR funded projects, **only where recruitment has been completed**. Examples include projects funded by UKRI (e.g. MRC, Innovate UK), Wellcome and major charities. All projects must have been through an external peer review process and we may request evidence of this. The remit would also include NIHR/MRC/Wellcome or equivalent **fellowships**, provided the sample sizes are sufficiently large. Alternatively, samples from fellowships could be incorporated into a larger pool of samples.

Applicants must provide evidence of data sharing agreements with the owner(s) of any data required for the proposed mechanistic study or agreement from the chief investigator of the original study if it was NIHR-funded. If the original chief investigator is not the chief investigator or a co-applicant on the mechanistic study, then permission must be obtained before applying and a supporting letter will be required at Stage 2.

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 intervention, future wealth creation and for the ultimate benefit of individual patients' or the wider NHS.

For standalone mechanistic studies please also provide the **project number, title, funding programme and award dates** of the study providing the patients/data/samples.

It is anticipated that applications to this call for mechanistic studies will be valued up to £350,000; however, there is no formal upper or lower limit. For all applications value for money is the key consideration.

Highlight notice

The NIHR programmes currently have the following highlight notice open:

Brain Tumours. This highlight notice indicates the continuing interest of NIHR in receiving research proposals in this area, and it encourages collaborative applications that demonstrate how they build on recent initiatives and investment in the area made by the NIHR, the MRC and other research funders.

For further details, please see the themed calls pages.

Please note that the EME Programme 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?