

IMPORTANT INFORMATION & GUIDANCE NOTES – PRELIMINARY APPLICATION

There are two different Efficacy and Mechanism Evaluation (EME) applications – PRELIMINARY application and FULL proposal.

The EME programme accepts PRELIMINARY applications in the first instance.

This document contains information and guidance to applicants submitting a PRELIMINARY application and is comprised of three parts;

- **Part One – Information about the EME programme** (pages 2-4)
- **Part Two - Completing your EME application form** (pages 5-8)
- **Part Three – Submitting your application** (page 9)

Applications which are not fully or correctly completed will be rejected.

Applications must be received by **Tuesday 16th March 2010 (before 1pm)**, in order to be considered at the June 2010 Board meeting.

Data Protection Act (1998): The Efficacy and Mechanism Evaluation (EME) programme is funded by the MRC and managed by the NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC) based at the University of Southampton. NETSCC has a contract with the Department of Health to manage the EME programme on its behalf.

Your name and address and other personal information that you provide will be held on a database in our password protected network. Your details and those of your co-applicants will be retained in order to facilitate the running of the EME programme. If your application is successful, at any stage of our process, your name and organisation details will appear on the EME website (www.eme.ac.uk). In addition, once funding has been agreed and the contract signed, your details will appear in other EME literature as a grantholder and may be passed to the NIHR and/or the MRC as appropriate. Your name and those of your co-applicants will be put on our mailing list. We may send you information about the EME programme and related events in healthcare research.

For any queries or concerns about the use of your personal data, please contact info@eme.ac.uk

PART 1 – Useful Information for Applicants

Introduction

The Efficacy and Mechanism Evaluation (EME) programme was launched in April 2008. It was created as part of the new National Institute for Health Research (NIHR) and the Medical Research Council (MRC) joint arrangement for clinical trials. The EME programme is managed by the NIHR as the lead organisation for clinical trials and evaluation, and funded by the MRC. The EME programme is broadly aimed at supporting 'science driven' studies with an expectation of substantial health gain. The clinical studies are likely to be mostly randomised controlled trials but other forms of evaluation appropriate for the intervention under study will also be supported.

Remit

The EME programme aims to support excellent clinical science with an ultimate view to improving health or patient care. Its remit includes clinical trials and evaluative studies - in patients - which:

- evaluate clinical efficacy of interventions (where proof of concept in humans has already been achieved);
- add significantly to our understanding of biological or behavioural mechanisms and processes;
- explore new scientific or clinical principles;
- include the development or testing of new methodologies.

The EME programme WILL support:

- research which seeks to determine definitive proof of clinical efficacy and size of effect, safety and possibly effectiveness;
- studies that use validated surrogate markers as indicators of health outcome;
- laboratory based, or similar, studies that are embedded within the main study, if relevant to the remit of the EME programme.

The EME programme WILL NOT support:

- confirmatory studies or trials of incremental modifications and refinements to existing medical interventions;
- proof-of-concept, proof-of-mechanism in humans, nor 'confidence in effect' studies;
- research into 'global health', where 'global health' can be defined as 'areas where the health need is identified in developing countries (i.e. including diseases of developing countries), or where the health need does not yet exist in the UK but might in the future and the problem can be best addressed in developing countries';
- research involving animals.

The EME programme will support research proposals which are important to healthcare, from researchers based across the UK.

Applications to the EME Programme

Preliminary applications will be accepted on an ongoing basis. There are, however, cut-off deadlines for applications to reach the EME offices so they can be assessed. Applications received after the stated deadline will not be considered in the next assessment round and will be held over for consideration in a future cycle. Please see the EME website (www.eme.ac.uk) for further information and updates on future deadlines and details of our assessment process.

Preliminary applications which are considered to be outside of the EME programme remit, non-competitive for funding or for which the application form has been incorrectly completed, will be rejected without further consideration. Applicants that are successful at the EME Board will be invited to develop their preliminary applications into full proposals for a subsequent Board.

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Required Expertise

Clinical and evaluative studies are typically multi-disciplinary enterprises and are likely to draw on the expertise of numerous disciplines. The EME programme recommends that teams proposing randomised controlled trials **include input from an accredited clinical trials unit**, or one with equivalent experience. A commitment to team working is encouraged and applicants should consider a collaborative approach between several institutions.

Research Networks

The EME programme expects that applicants will work, where appropriate, with the relevant NIHR Clinical Research Network (www.ukcrn.co.uk).

Public Involvement

Patient and public involvement (PPI) is important and will be actively sought across the EME programme. Evidence of PPI involvement will be sought in applications and on Trial Steering committees and comments from public and patient reviewers will be regularly obtained.

The EME programme recognises the increasing active involvement of members of the public in research and would like to support research projects appropriately. The EME programme encourages applicants to consider *how* the scientific quality, feasibility or practicality of their proposal *might* be improved by involving members of the public. Research teams wishing to involve members of the public should include in their application: the aims of active involvement in this project; a description of the members of the public (to be) involved; a description of the methods of involvement; and an appropriate budget. Applications that involve members of the public will not, for that reason alone, be favoured over proposals that do not but it is hoped that the involvement of members of the public will improve the quality of the application.

INVOLVE (www.invo.org.uk) is a National Advisory Group funded by the Department of Health, which aims to promote active public involvement in NHS, public health and social care research. INVOLVE have published a number of documents aimed at researchers seeking to involve the public in their research including:

- [Involving the public in NHS, public health, and social care research: Briefing Notes for Researchers](#)
- [Suggested guidance for grant applicants about involving the public in research](#)
- [A guide to reimbursing and paying members of the public who are actively involved in research: For researchers and research commissioners \(who may also be people who use services\)](#)

INVOLVE also produce a useful publication aimed at members of the public wishing to get actively involved in research (other than as a trial participant) [Getting Involved in Research - a Guide for Consumers](#). Researchers should also use this as a resource for advice on involving the public in research.

Governance and Regulation

Applicants are asked to:

1. Follow the Medical Research Council's Good Clinical Practice guidelines (www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002416) in planning how studies, particularly RCTs, will be supervised.
2. 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

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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, www.mhra.gov.uk) can provide guidance as to whether your trial would be covered by the regulations. The Department of Health/MRC website (www.ct-toolkit.ac.uk) also contains the latest information about Clinical Trials regulations and a helpful FAQ page.

Criteria for Assessment

In its assessment of applications, the EME Board is likely to use the following criteria:

1. *Scientific quality of the proposal including:*

- a) *What is the likelihood of a study making a substantial advance in scientific understanding and knowledge?*
- b) *What is the likelihood of the study leading to a substantial health gain?*
- c) *What is the likelihood of the study increasing our understanding of the broader topic area?*

2. *Feasibility of the study*

- a) *Demonstration of the necessary skill mix, experience, project management and infrastructure for success*
High quality clinical and evaluative studies need a multi-disciplinary team. Applicants need to show a commitment to team working and may wish to consider a collaborative approach between several institutions. The EME programme recommends applicants to engage an experienced trial manager for appropriate projects. It is important to involve service users.
- b) *Explanation and justification for estimated recruitment rates.*
The EME programme wants studies to achieve their aims. Researchers should demonstrate that they can recruit the necessary number of participants.
- c) *Ethical, legal and social implications of the research proposed have been considered.*

3. *Reasonable costs and value for money.*

There are no fixed limits on the duration of projects or funding and proposals should be tailored to fully address the problem.

Further Information

Further information on applying to the EME programme is available from the Frequently Asked Questions (FAQs) section on the EME website (www.eme.ac.uk). Please email any queries to info@eme.ac.uk

PART 2 - Completing Your Electronic Application Form

To submit a preliminary application you must complete all of the sections on the web form and provide a flow diagram illustrating the study design and flow of participants (as a .pdf file). Applicants are limited to the space provided on the webform (not a word count), and an approximate number of characters that may fit in the space provided is included in the relevant online help files, indicated by a '?' icon next to the entry fields. Please note that this is based on all available space on the form being fully utilised.

Please note that, the EME programme will only accept and consider preliminary applications submitted via the form on the website accompanied by a single flow diagram (1 page A4, submitted as a PDF). Any other documents submitted will be removed and not considered in the assessment process.

Before you begin:

It is advisable to save your form soon after you begin. To do this, click save and follow the instructions, making sure that you take note of your Save ID. If you send a colleague the save ID for the form they can access and make changes to your form. Please note that only one person can access the form at any one time.

Section A: Applicants

Details of Lead Applicant

Please complete all sections and state the contribution towards the proposed project (e.g. lead applicant, principal investigator, data collection, co-ordination and project management, analysis, methodological input, consumer input). Please note that all correspondence will be addressed to the lead applicant.

Details of Joint Applicants

Please use the "add applicants" button to complete personal details for all joint applicants (do not resubmit details for the lead applicant in this section) and state their contribution towards the proposed project (e.g. data collection, co-ordination and project management, analysis, methodological input, consumer input). Please note you are limited to **a maximum of 12 joint applicants, including the lead applicant**, at this stage. If you are invited to submit a full proposal you will be given the opportunity to increase the size of your team.

Do not include collaborators (individuals who will contribute to the research but do not have responsibility for its management) in this section. You will have the opportunity to include them at the full proposal stage.

Section B: Project Details

Classification of Research: Please use the drop down list to indicate which **one** 'International Statistical Classification of Diseases and Related Health Problems 10th Revision' (ICD-10) Chapter is the most appropriate classification for your proposed research. This information will be used to monitor the areas of research which are proposed to the EME programme, as well as assisting with its processes. Further information on ICD-10 can be found at www.who.int/classifications/apps/icd/icd10online

NHS Region/Country: Please select the NHS region/country in which the lead applicant's organisation is located. Applicants must note that lead applicants to the EME programme must be based in the UK. Co-applicants may be based outside the UK, and if necessary research can be conducted overseas. The rationale for this should be clearly set out in the application and each case will be judged on its merits.

Start Date: Please note that successful projects are expected to start within a reasonable time following a decision to fund.

Research costs and total research costs including NHS costs: Please enter the total amount estimated at this stage. Applicants from Higher Education Institutions should enter the research grant figure as 80% of the full economic cost. Applicants from other organisations (such as NHS Trusts) should enter 100% of the research cost. Inflation should only be applied to salary costs, as should known pay awards and incremental rises.

At the full proposal stage, applicants will be required to detail costs in relation to all personnel, travel and subsistence, equipment, consumables, and other direct costs. Higher Education Institutions will be required to include estates charges and other indirect costs (based on TRAC methodology).

Applicants should note that it is in their interests to undertake a thorough, realistic and accurate costing. The EME programme expects that costs identified should not differ between outline and full proposal stage. The Board will pay close scrutiny to increases and applicants must provide a clear and full justification for any differences.

Although there is no limit to the amount of money you can ask for in one proposal, applicants should be aware that they will be competing for limited funds.

NHS Support Costs and estimated treatment costs (including excess treatment costs) should be added to the total research costs to give 'research costs including NHS costs'. The EME programme will only pay research costs.

Clinical Trials Unit Registration: Please tick if the CTU involved has received either full or provisional registration from the NIHR Clinical Research Network (NIHR CRN). Please note this information is for internal processes only and will not be used in the assessment of your application.

Clinical Trials Unit Infrastructure Funding Information: Please tick if your application involves a Clinical Trials Unit (CTU) and this CTU is in receipt of NIHR CTU Infrastructure Support Funding. Please specify the CTU. Please leave blank if not applicable. Please note this information is for internal processes only and will not be used in the assessment of your application.

Clinical Trial Authorisation (CTA): Please tick the box if CTA is required. The MRHA have published information, and an algorithm, to help in identifying whether a trial should be managed within 'The Medicines for Human Use Regulations 2004'. Please see www.mhra.gov.uk for further information.

Section C: Non-expert Summary

Please provide a summary in plain English suitable for a non-expert that will enable them to understand the research question and the project you are proposing. The summary should enable the non-expert reviewer to understand the following;

- how the proposal addresses the research proposed,
- how and where the research will be carried out,
- what outcomes will be used to assess the success of the research,
- what (if any) are the ethical issues involved in this study and the arrangements for handling these,
- why this team is well placed to carry out the research,
- and provide a justification for the costs requested (including any NHS costs).

Please ensure that you only include acronyms where necessary and that these are defined within the text. More detail on writing for public consumption is available from the Plain English Campaign. A free guide designed specifically for the Health Sector can be found at: www.plainenglish.co.uk/medicalguide.pdf

Section D: Expert Summary

Please provide a summary of your proposed research. This should not be written in the same style as the non-expert summary. Please include the hypothesis and aims, design, population, interventions, outcomes, assessments, sample size, statistical analysis and economic benefit. You should also describe the expertise of the team.

Section E: Hypothesis and Aims

Please state your hypothesis(es) and aims. Please also list the research questions that your proposal seeks to address (in question format).

Section F: Project Details and Justification

F1. Remit

Please explain how your proposed research is within the remit of the EME programme. You should include a clear explanation of the main (single) research question phrased in PICO terms (Population; Intervention; Comparator; Outcome). Give a brief explanation of how or in what ways the design constitutes a clinical trial or evaluation study. You are welcome to highlight any other aspects of the design that you would like to bring particular attention to, in order to explain how it is within remit. Please remember that EME research looks at patients or people seeking healthcare; studies using healthy volunteers and animals are not within the remit of the programme.

F2. Background and References

Please provide a clear explanation of the health problems to be addressed, the impact on patients and healthcare, an explanation of the scientific principles of the proposed research and an overview of the potential economic benefits (you are not required to include health economics analysis within your research). You should give reference to any relevant systematic reviews and discuss the need for your trial in light of these. If you believe that no relevant previous trials have been done, give details of your search strategy for existing trials. Please give details of other trials currently underway, both nationally and internationally, which are relevant to the proposed study. Please explain why this trial is needed now. References should be provided in the Vancouver format (*Author(s). Title. Journal. Year; Volume: Start page - End page*).

F3. Brief Description of Project Protocol

Please provide a brief description of your project protocol, based on the headings below. If your preliminary application is successful, you are likely to be able to expand this information for a detailed project description at the full proposal stage. Please ensure that all acronyms are defined within the text.

- **Research design**
Give a brief statement on the type of study design to be used.
- **Study population**
Please provide a description of the planned inclusion/exclusion criteria.
- **Planned interventions**
Include both experimental and control interventions.

- **Proposed outcome measures**
Detail both the primary and secondary outcomes. Validated surrogate markers are acceptable, where appropriate.
- **Assessment and follow up**
Please provide details of how / when outcomes / safety will be assessed.
- **Proposed sample size**
Specify the number of patients and centres (including both control and treatment groups). Give details of the estimated effect size, power and/or precision employed in the calculation. A justification of the estimated effect size and the assumptions underlying the sample size calculations must be provided.
- **Statistical analysis**
Clearly state the purpose of any statistical analysis, and do not simply name a statistical test or software package. The proposed type and frequency of analyses must be stated including the selection of participants to be included in the analyses. Describe any planned interim and sub-group analyses.
- **Project timetables including recruitment rate**
Indicate the anticipated duration of the study, paying particular attention to the expected recruitment rate and a justification for your estimate. Outline the main stages of the proposed project with expected durations.

F4. Justification of Costs

Please give a brief justification of the total cost of your research. At the full proposal stage, applicants are required to provide detailed financial information on staff, travel and subsistence, equipment, consumables, other direct costs, indirect costs (only applicable to Higher Education Institutions), and NHS costs.

Section G: Collaboration

The EME Board expects that applicants will work, where appropriate, with the relevant NIHR Clinical Research Network(s), see www.ukcrn.co.uk. Please state which network(s) you intend to work with and indicate the level of progress in developing this and potential benefits identified to date, supplying as much detail as you can.

Section H: Team Expertise

Outline the particular contribution each member of the team will make towards the project. The team should be multidisciplinary and include all relevant expertise to enable delivery of the proposed research. The EME programme recommends teams proposing randomised controlled trials to include input from an accredited clinical trials unit or one with equivalent experience.

The EME Board welcomes information on your or your team's wider research activities. We are particularly keen to hear about how your previous or current work will fit with this application.

Section I: Key Information

I1. If you are proposing a study which requires joint or shared funding, it is in your interests to provide a clear explanation of the arrangements for this.

I2. Please note that the EME programme will not accept applications that are currently pending with other research funding organisations (unless under shared funding arrangements).

13. Please provide full details on any patents (or other exploitable results) that may arise from the research.

14. Please declare any interests that you or any of your other applicants might have. This includes, but is not limited to, any facts that, should they come to light at a future date, would embarrass either the programme or the individual who withheld the fact (e.g. if a member of the team holds a patent or has a financial interest within the research area).

15. Please provide details if applicable.

Section J: Referees

If your preliminary application is selected for consideration by the EME Board it will be subject to external review by one clinical expert. You should provide details of three clinical experts who will be able to provide an independent assessment of your proposal. Please note that the referees may not be from your host institution, or those of your joint applicants. In addition you should not have recently (within the last five years) collaborated with any of the nominated referees. It is permissible to nominate experts overseas.

Nominated referees who are acceptable to the EME programme will be approached approximately two weeks after the submission deadline. If they are willing to assist, they will be supplied with a copy of your proposal, an assessment form and guidance notes, and will be given a 2-3 week period to complete their review. **Please take care to complete the tick box at the bottom of the page to provide assurance that the experts listed have agreed to this nomination.** You may also use the form to tell us about people you would prefer us not to approach as referees.

FLOW DIAGRAM

Finally, please create a flow diagram (single-side of A4), as a separate .pdf file, for submission with your application form. This should illustrate the study design and the flow of participants. Applicants should also describe complex interventions and controls as accurately and fully as possible within their diagram. If proposing an RCT, we advise you refer to the CONSORT statement and website for guidance (www.consort-statement.org). Alternatively, you may find the EQUATOR Network website useful (www.equator-network.org). The .pdf file should be submitted along with your application form (details are provided in Part 3 of this document).

PART 3 – Submitting Your Application

The EME programme requires an electronic copy of your application form and flow diagram .pdf to reach our offices by the stated deadline in order to process your application in the next round. Please note that we cannot grant any time extensions.

The deadline for the next round is Tuesday 16th March 2010 (before 1pm).

Please ensure that before you submit your application, you have completed the necessary fields and saved a version of your form.

When you submit your form with the flow diagram it will be emailed to the EME offices.

If you encounter problems when submitting your form you can contact the team at the EME programme using the telephone numbers provided at the bottom of the application form and giving the identification number of the form. This will enable the team to see your form while they are speaking to you, but not to make changes.

Confirmation of receipt: The EME programme will acknowledge all submissions by email. If for any reason you are concerned that your submission has not reached us, please contact a member of the team at info@eme.ac.uk or on 023 8059 4303.

The secretariat, in consultation with the Programme Director and Chairman of the Board, will undertake initial checks on all preliminary applications submitted to ensure that they are within the programme remit and are therefore eligible for consideration. Applications which do not fulfill this criterion will be rejected at this stage.

Preliminary applications which are within remit will also be assessed on overall quality and the likelihood of meeting the fundable criteria when assessed by the EME Board. Applications which are not considered to be competitive for funding will be rejected at this stage.

We expect to be able to inform all lead applicants as to whether or not their preliminary application will be considered by the Board within 2-3 weeks of the submission deadline.

If, after carefully reading all the instructions, you still have difficulties completing your application, please visit the EME Programme website (www.eme.ac.uk) which contains a list of Frequently Asked Questions (FAQs) and answers. If your particular query or problem is not addressed, please telephone 023 8059 4303 or email info@eme.ac.uk. A member of the team will contact you as soon as they are able to.