HTA Clinical Evaluation and Trials: an Open Call

Specification Document

Introduction
The NIHR Health Technology Assessment programme is funded by the NIHR, with contributions from the Chief Scientist Office (CSO) in Scotland and National Institute for Social Care and Health Research (NISCHR) in Wales. Researchers from Northern Ireland should contact NETSCC to discuss their eligibility to apply.

The NIHR Health Technology Assessment programme funds research to assess the effectiveness of technologies within the NHS. In this researcher-led work-stream grants are available for primary research and evidence synthesis on topics proposed by the researchers. We accept outline proposals on an ongoing basis. There are four deadlines a year.

Further information on HTA researcher-led call is available from a Frequently Asked Questions section on the HTA website (http://www.hta.ac.uk/funding/troubleshooting/clinicaltrials.html). Please email any queries to htacet@soton.ac.uk.

Type of proposal invited
Proposals should normally evaluate the clinical and cost effectiveness of a health technology. For diagnostic technologies, researchers may suggest equivalent evaluations.

We are interested in receiving proposals addressing any health problem in areas not otherwise well covered in our portfolio (please see http://www.hta.ac.uk/). Please note that proposals should be within the remit of the HTA programme, so proposals to investigate the organisation of health services, or services entirely outside the NHS will not be eligible.

Technologies to be investigated
The HTA programme undertakes research for the benefit of patients and the NHS. Health technology covers any method used to promote health, prevent and treat disease and improve rehabilitation or long-term care. 'Technologies' in this context are not confined to new drugs or equipment, but include procedures, devices, tests, settings of care, screening programmes and any intervention used in the treatment, prevention or diagnosis of disease. They should be currently used in the NHS, or likely to be used if supported by the results of the research. Technologies being evaluated should have had some assessment of efficacy already. For less well evaluated technologies consider the EME programme (see www.netscc.ac.uk/funding/technology_evaluations.asp). Proposals to evaluate public health interventions in other settings may be eligible to apply to the Public Health Research programme (www.phr.ac.uk).

Study designs
The programme does not restrict the study designs it will consider, but they must be the most suitable to answer the specific HTA research question. Applicants should justify their design.

For primary research projects (which generate new data) the most suitable study design is often a randomised controlled trial, but this is not the only type of trial we fund. Other study designs may be appropriate, for instance cohort or other observational studies, or adaptive designs. All should be adequately powered and the results should be relevant across the UK population.

Feasibility and Pilot studies are eligible. We expect that when pilot or feasibility studies are proposed by applicants, or specified in commissioning briefs, a clear route to the substantive study will be described. This applies whether the brief or proposal describes just the preliminary study or both together. Whether preliminary and main studies are funded together or separately may be decided on practical grounds.

Feasibility Studies are pieces of research done before a main study. They are used to estimate important parameters that are needed to design the main study. Feasibility studies for randomised controlled trials may not themselves be randomised. Crucially, feasibility studies do not evaluate the outcome of interest; that is left to the main study. If a feasibility study is a small randomised controlled trial, it need not have a primary outcome and the usual sort of power calculation is not normally undertaken. Instead the sample size should be adequate to estimate the critical parameters (e.g. recruitment rate) to the necessary degree of precision.

Pilot studies are a version of the main study that is run in miniature to test whether the components of the main study can all work together. It is focused on the processes of the main study, for example to ensure recruitment, randomisation, treatment, and follow-up assessments all run smoothly. It will therefore resemble the main study in many respects. In some cases this will be the first phase of the substantive study and data from the pilot phase may contribute to the final analysis; this can be referred to as an internal pilot. Or at the end of the pilot study the data may be analysed and set aside, a so-called external pilot.

For a full definition of the terms 'feasibility study' and 'pilot study' visit the NETSCC website www.netscc.ac.uk/glossary

Evidence synthesis projects are also eligible. These should investigate clinical and cost-effectiveness. They are likely to include one or more systematic reviews and economic analysis, but other well designed studies are eligible. Researchers can also apply to the Research for Patient Benefit programme for evidence synthesis studies. Researchers should justify why the HTA programme is the most appropriate to fund this study, rather than other programmes.

Criteria for assessment of proposals
Applications to the HTA Clinical Evaluations and Trials call are assessed in three stages; two for the outline and a further one for subsequent full proposals. Outline proposals are checked for eligibility and then undergo a two stage competitive assessment for:

a. the need for the evidence in the NHS
b. the scientific rigour of the research.

Need for evidence
Outline proposals will first be prioritised for NHS need by a panel of experts, using the following criteria.

1. *The importance of the health problem to patients and the NHS*. Applicants should describe the burden (frequency and severity) of the health problem in the population and the potential benefit from the technology.
2. *The relevance of study outcomes to patients and the NHS, and the relevance of participants to the case mix treated in the NHS.* Clinically important outcomes that matter to patients and that measure health gain should be used. These will usually be long-term. Widely accepted surrogate markers may be used if they are strongly linked to health outcomes. For primary research, participants should reflect the mix of patients likely to be seen in normal clinical practice.
3. *Justification of proposed research with reference to the current evidence base*. The importance of the research question to the NHS should be explained. Researchers should describe the current level of uncertainty and how their research will reduce it. This should include an account of the existing evidence, and any relevant research being undertaken in the HTA programme and elsewhere. The applicants should consider evidence in

related technologies, diseases or patient groups when justifying their proposal. A systematic review should normally have been undertaken before a trial is considered.

4. *The technology assessment is relevant to the NHS.* There should be an adequate description of the technology and its possible effectiveness range. It must be one that is used in the NHS, or could be adopted into the NHS following the study. The study should usually assess cost-effectiveness in the NHS or justify this omission.

Scientific rigour
Selected proposals are then considered by the HTA Clinical Evaluations and Trials Board. The Board uses the following criteria.

1. *Scientific quality of the proposal.* The proposal should be carefully designed to ensure good internal and external validity.

2. *Demonstration of the necessary skill mix, experience, project management and infrastructure for success.* High quality proposals need a multi-disciplinary team. The HTA programme expects research teams to have an appropriate mix of skilled people, such as partnerships between research clinicians and methodologists. For clinical trials, applicants are encouraged to include input from an accredited clinical trials unit, or one with equivalent experience and should plan to engage an experienced trial manager. A commitment to team working is important and a collaborative approach between institutions is welcome.

3. *Explanation and justification for estimated recruitment rates in primary research.* Studies should achieve their aims, including recruiting the necessary participants. In the case of clinical trials sample sizes are likely to be large. Researchers should demonstrate that they can recruit the necessary number of participants. The HTA programme welcomes studies based in settings with a track record of successful recruitment.

4. *Ethical, legal and social implications of the research proposed have been considered.*

5. *Reasonable costs.* The HTA programme includes 'value for money' in its assessment. The resources requested should be reasonable to answer the specific research question.

Successful outline proposals
Applicants who are successful at the HTA Clinical Evaluations and Trials Board will be asked to develop their outline proposals into full proposals, usually for the next but one board meeting.

Research networks
The HTA programme expects, where appropriate, that applicants will work with a relevant research network.

Public involvement
The HTA programme recognises the increasing active involvement of members of the public in research and would like to support research projects appropriately. The HTA programme encourages applicants to consider *how* the scientific quality, feasibility or practicality of their proposal *might* be improved by involving members of the public. Examples of how this has been done for health technology assessment projects can be found at http://www.hta.ac.uk/PPIguidance/. 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
- an appropriate budget.

Applications which involve members of the public will not for that reason alone, be favoured over proposals which 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 key organisation for promoting public involvement in research, in order to improve the way that research is prioritised, commissioned, undertaken, communicated and used. Researchers should use the INVOLVE web site for further details on involving the public in research.

Governance and regulation
Applicants are asked to consult the following documents and follow them as appropriate:

- Medical Research Council's Good Clinical Practice guidelines: http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002416. To be used when planning how studies, particularly RCTs, will be supervised. Further advice specific to each topic will be given by the HTA programme at full proposal and contract stages.
- Department of Health's Research Governance Framework for Health and Social Care http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4108962
- Department of Health/Medical Research Council Clinical Tool Kit http://www.ct-toolkit.ac.uk/

Note that trials or studies involving medicinal products must comply with The Medicines for Human Use (Clinical Trials) Regulations 2006 and the amendment to the regulations. In these cases, the DH 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 DH 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 DH 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, http://www.mhra.gov.uk) can provide guidance as to whether your trial would be covered by the regulations.

Timescale
Outline proposals to this open call will be accepted on an ongoing basis. There are, however, cut-off deadlines for proposals to reach the NETSCC, HTA offices so they can be assessed.

There are no fixed limits on the duration of projects or funding, and proposals should be tailored to fully address the problem. However, applicants should balance the pressing need within the NHS for the information with the need to follow up participants for long enough to measure important outcomes.

Making an application

- The Clinical Evaluation and Trials Application form can be found on our website at: http://www.hta.ac.uk/funding/clinicaltrials/howtoapply.shtml
- Before completing this form you should read the guidance notes which can be found on our website at http://www.hta.ac.uk/funding/clinicaltrials/howtoapply.shtml
- Applications received after **13:00hrs on 1 February 2011** will not be considered in this assessment round and will be placed into the next cycle for consideration at a later date.

Further questions

If you have any questions which have not been covered in these guidance notes, please visit our FAQ pages at www.hta.ac.uk/funding/troubleshooting/index.html .