HTA Clinical Evaluation and Trials: an Open Call

Specification Document

Introduction
The Health Technology Assessment (HTA) Programme is part of the National Institute for Health Research (NIHR). The secretariat function of the programme is managed by the NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC) based at the University of Southampton under a contract with the Department of Health.

The Health Technology Assessment Programme is funded by the NIHR, with contributions from the CSO in Scotland, NISCHR in Wales, and the HSC R&D Division, Public Health Agency in Northern Ireland.

The NIHR HTA 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.

Changes to application process
Primary research applicants will continue to complete an outline application form; if the outline is successful a full application form will be invited.

Evidence synthesis applicants will now be required to apply via a full proposal form, available on the website.

We accept proposals on an on-going basis. There are three deadlines per year.

Further information on the HTA researcher-led call is available from a Frequently Asked Questions section on the HTA website at: 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/). However, for the cut-off date of **1pm on Monday 7 January 2013* the National Institute for Health Research (NIHR) is inviting applications for research into interventions for Very Rare Diseases, please see the separate document available on the website for the full detail of this topic focus.** Please note that proposals should be within the remit of the HTA Programme (please see http://www.hta.ac.uk/funding/remit.shtml).
Proposals to investigate the organisation of health services, or services entirely outside the NHS will not be eligible.

***Please note that we will be accepting all proposals relevant to the Clinical Evaluation and Trials work stream, as well as for the topic focus.**

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, please see the following link: (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 (please see 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 and note that we are unlikely to support single centre studies which are less likely to give results applicable in a large number of NHS settings.

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, a clear route to the substantive study will be described. This applies whether the 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 at: www.netscc.ac.uk/glossary

Evidence synthesis projects are also eligible; please note that applicants can now complete a full proposal form for evidence synthesis projects, ensuring a faster funding decision is reached. 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
Primary research applications to the HTA Clinical Evaluation and Trials call are assessed in three stages; two for the outline proposal and a further one for subsequent full proposals. Evidence synthesis full applications will be assessed in two stages.

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
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.
   - Where established Core Outcomes exist they should be included amongst the list of outcomes unless there is good reason to do otherwise. Please see The COMET Initiative website at www.comet-initiative.org to identify whether Core Outcomes have been established.
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 Evaluation 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 Evaluation and Trials Board will be asked to develop their outline proposals into full proposals, usually for the next 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

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

- To access the form please go to: http://www.hta.ac.uk/funding/clinicaltrials/index.shtml
- Before completing your form you should read the guidance notes which can be found on our website at: http://www.hta.ac.uk/funding/clinicaltrials/index.shtml
- Applications received after **1pm on Monday 7 January 2013** 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 .