Open Call for proposals in the area of Medicines for Children

Introduction

NHS R&D has funded the creation of the Medicines for Children Research Network (MCRN) to support the development of safe and effective medicines for use in the treatment of children. The remit of the NHS R&D Health Technology Assessment (HTA) programme with this Call is to promote high quality research on the effectiveness and broader impact of health technologies in this area. The HTA programme wishes to help support the start of the network by funding evaluative and methodological research by investigators from a wide range of disciplines.

Definition of Medicines for Children

All medicinal products used in the age range of newborn to eighteen years old.

Type of proposal invited

As an open Call the following types of proposed research are invited; primary research (RCTs or other studies), secondary research and methodological studies. Proposals will need initially to fall within the remit of the HTA programme. Proposals will be assessed against this criterion before reaching the Board convened to assess the proposals. Normally the HTA programme funds cost-effectiveness research. In this Call however, the focus is being broadened and need not include costs. Nevertheless, as a minimum, it must include an evaluation of the effectiveness of a health technology in terms of children's health (or associated methodological questions).

The Board will then assess against the following criteria (as reflected in the proposal form).

1. Importance of the health problem (including its relationship to government/NHS strategy and policy)
2. What outcomes matter most to children and families and how these should be measured.
3. The technology or method and its possible effectiveness range.
4. Current evidence base.
5. Current use of the technology or method and its likely diffusion.
6. Views of those working in and using the NHS.
4. Scientific quality.
5. Value for money

Further guidance on submission

Primary research

The MCRN has advised the HTA programme that there are three main areas for this Call where it would be appropriate to undertake clinical trials of drugs through the network.

1. Trials of drugs which are currently in-patent and unlicensed for use by children but which are licensed and used in adults. This may include the development of suitable paediatric formulations and studies of bioavailability and pharmacokinetics.
2. Trials of drugs which are off-patent and unlicensed for the treatment of children. This will often include development of suitable paediatric formulations and studies of bioavailability and pharmacokinetics.
3. Novel uses of drugs that are currently licensed for use in children.

It is anticipated that the network will predominately be involved with Phase III trials however they accept that for some drugs the pharmacology of drug in children will need to be assessed and so require early phase studies. The HTA programme is supportive of a staged approach to some of these key questions and the need to design a proposal such that the research involves identifying a first question which needs to be answered before research on a subsequent one should start. We expect that the usual pre-requisite for a clinical trial would be a high quality systematic review.

Methodological research

Proposals for methodological studies are welcomed. There are many areas where the methodology for undertaking clinical trials and observational studies with children is poorly developed, or existing methods are inadequate. There may be difficulties in applying methodologies developed in other fields to children or a lack of a suitable methodology.

Secondary Research

Proposals for secondary research topics are welcomed where they are likely to make a major impact on patient care.

Applicants should consider:

Networking

It is anticipated that multicentre clinical studies (including clinical trials) funded from this call will be conducted through the MCRN. The MCRN has resources, specifically a dedicated Medicines for Children Clinical Trials Unit, with which applicants may wish to consider collaborating. Further information is available at http://www.liv.ac.uk/mcrn/. The MCRN will not provide comments to applicants at the outline stage but will provide comments on applications which are shortlisted.

Ethical, Legal and Social Issues

All those involved in research with children must adhere to the strictest ethical and legal standards. Ethical, social and legal issues must be considered in relation to all stages of the research cycle. Applicants are asked to consider documents such as the MRC Ethics Guide: Medical research involving children (2004); the DH document: Seeking Consent, Working with Children (DH 2001). Applicants should follow the Medical Research Council's Good Clinical Practice guidelines (http://www.mrc.ac.uk/pdf-ctg.pdf) when planning how studies, particularly RCTs, will be supervised.

Regulation

Note that trials involving medicinal products must comply with European Union Directive 2001/20/EC. For trials covered by the Directive the DH, with the HTA programme acting as their agent, is prepared, *in principle*, to be nominated as the sponsor. The responsibilities of the sponsor, as indicated by the directive, will then be agreed amongst the HTA programme, the host institution and the successful applicant. The DH reserve the right to withdraw from the role of sponsor if they are not satisfied with the arrangements put in place to conduct the trial. Experience shows that some host institutions prefer to assume the role of sponsor for purposes of the EU Clinical Trials Directive [2001/20/EC]. This is consistent with their duties and responsibilities under the Research Governance Framework and the HTA programme would support this approach.

If you are not clear as to whether your trial would be covered by the directive you should contact the MHRA (info@mhra.gsi.gov.uk) for help in this matter.
Their website (http://medicines.mhra.gov.uk/ourwork/licensingmeds/types/clintrialdir.htm) contains the latest information about the EU Clinical Trials Directive [2001/20/EC] and a helpful FAQ page.
The MHRA have developed an influential paediatric strategy (http://medicines.mhra.gov.uk/ourwork/licensingmeds/children/children.htm#ukstrat) to which all potential triallists should refer.

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. 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.

Three organisations key to this call encourage researchers to involve the public in their work:

The **UK Clinical Research Collaboration** (UKCRC - *http://www.ukcrc.org/*) is a new partnership with a shared vision to establish the position of the UK as a world leader in contributions to clinical research by harnessing the power of the NHS. It will engage and consult with patients throughout its activities, in particular through engagement with INVOLVE and the Association of Medical Research Charities. Under the strategic oversight of the UKCRC, the UK Clinical Research Network Coordinating Centre (UKCRNCC - http://www.ukcrn.org.uk/) consists of a managed set of Topic Specific Research Networks, including one in the area of Medicines for Children.

The **Medicines for Children Research Network Coordinating Centre** (MCRNCC - http://www.liv.ac.uk/mcrn/), working with the UKCRNCC, encourages the involvement of children in guiding research. MCRNCC will work closely with INVOLVE and the National Children's Bureau to address the issues relevant to the involvement of children and parents in all aspects of the research process.

Both the UKCRNCC and the MCRNCC have partnerships with **INVOLVE (***http://www.invo.org.uk/***),** a key organisation for promoting public involvement in research, in order to improve the way that research is prioritised, commissioned, undertaken, communicated and used. By doing so, it is hoped that such research will be more relevant to the public's needs, more reliable and more likely to be used. INVOLVE have published a number of documents aimed at researchers seeking to involve the public in their research:

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 Paying Members of the Public Actively Involved in Research

A Guide to Actively Involving Young People in Research: for researchers, research commissioners, and managers

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.

Required expertise

HTA is a multidisciplinary enterprise. It may need to draw on the expertise and knowledge of clinicians and of those trained in health service research methodologies such as health economics, medical statistics, study design and qualitative approaches. HTA expects applicants to engage a qualified Trial Manager for appropriate projects. Applicants will need to show a commitment to team working and may wish to consider a collaborative approach between several institutions.

Timescale

There are no fixed limits on the duration of projects or funding and proposals should be tailored to fully address the problem. However, there is a pressing need within the NHS for the information and so the research would normally be expected to be completed within a reasonable time.

Making an application

If you wish to submit an outline proposal on this topic, complete the electronic application form and return it to the Commissioning Manager at the National Coordinating Centre for Health Technology Assessment, Mailpoint 728 Boldrewood, University of Southampton, Southampton SO16 7PX by **19th October 2005**. Outline applications will be considered by the Medicines for Children Assessment Board at its meeting in December 2005. If the outline proposal is acceptable, investigators will be given a minimum of eight weeks to submit a full proposal.

Applications received after 1300 hours on the due date will not be considered.