ENZYME REPLACEMENT THERAPY FOR LYSOSOMAL STORAGE DISORDERS

Introduction

The aim of the HTA programme is to ensure that high quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and work in the NHS. Health technology assessment forms the largest portfolio of work in the NHS Research and Development Programme and each year about forty new studies are commissioned to help answer questions of direct importance to the NHS. The studies include primary and secondary research and cost about £10 million a year. Questions are identified and prioritised to meet the needs of the NHS and its patients.

Research overview

Research on this topic is to be undertaken as two consecutive projects. This commissioning brief describes the first of these (Part 1). Part 2 will be commissioned separately, although the expectation is that this will be with the same team, based on the output from Part 1 (a full proposal).

The task in Part 1 is to design an appropriate longitudinal study to determine the effectiveness and cost effectiveness of enzyme replacement therapy (ERT) for lysosomal storage disorders (LSD). The output of this part will be a full proposal.

At this stage we are seeking a short outline (2 sides of A4), a brief summary of the work required to develop a full proposal, together with proposed costs. It is anticipated that this work will include:

- An overview of the existing evidence. The HTA programme has commissioned a research synthesis report, which will inform this task.
- Establishing a working arrangement with the clinicians
- Examining the existing disease registers and their possible role in the study
- Identifying appropriate clinical and economic outcome measures
- Identifying potential comparator groups
- Linking with the process being developed by NICE to appraise orphan drugs including ERT.
- Developing a study protocol.

Research required

The proposal for Part 2 is expected to include the following; however the investigators may modify these if justified by the work of Part 1.

1. **Technology:** Enzyme replacement therapy for lysosomal storage disorders as provided under the national designation (http://www.dh.gov.uk/assetRoot/04/09/22/10/04092210.pdf)

2. **Patient group:** Patient groups eligible for therapy under the national designation.
3. **Control or comparator data:** Means of assessing the natural history of conditions without treatment will need to be clearly defined but may use relevant historical data.
4. **Design:** A longitudinal study that will capture and build on existing data. The design should be specified in detail in the protocol including include methods of data collection and analysis.
5. **Primary outcomes:** Patient-centred measurable outcomes that will be useful to policy makers and help populate an economic model should be identified. It will be important to estimate the benefits of treatment on quality of life. Biochemical or other markers of disease progress will not be sufficient. Costs should be measured with a view to assessing cost-effectiveness of treatment.
6. **Length of follow-**up: Five to ten years.
7. **Researchers and collaborators:** Key collaborators including the six lead consultants should be identified and agree to be actively involved in the study proposed

Summary of research need:

LSDs are rare genetic diseases and the treatment is very costly. The Department of Health has agreed to fund the treatment of LSDs for a period of two years from April 2005. Assessment, therapy and associated support will take place in six designated hospitals and involve six lead consultants. This service is being commissioned by the National Specialised Commissioning Advisory Group (NSCAG) at the DH.

A synthesis of research commissioned by the HTA programme is near completion. This will identify the important gaps in evidence and the research needs on this topic. A prospective longitudinal study is required to assess the effectiveness and cost-effectiveness of this treatment.

The small number of patients and the lack of a potential parallel control group provide important challenges to studying this topic. Therefore the HTA programme wishes to commission a scoping study in the first place, which will lead to the proposal for the substantive study. Once the proposal has been approved we would expect the substantive study to be undertaken according to the proposal and by the team outlined in the study proposal.

Any queries on this commissioning brief should be addressed to Pauline Swinburne, External Projects Manager at the National Coordinating Centre for Health Technology Assessment, Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX (email: Pauline@soton.ac.uk).

Guidance on applications

Methods

Applicants are asked to:

1. Provide a two page document briefly summarising the work required to develop a full proposal, together with proposed costs by the 24th February. This will be reviewed internally and the applicants notified early in March 2005 of any decision to commission.

2. Note that any proposed study in this area must comply with European Union Directive 2001/20/EC. Clinical trial authorisation must be obtained from the MHRA and any study design will need to satisfy their requirements. For further information their website (http://medicines.mhra.gov.uk/ourwork/licensingmeds/types/clintrialdir.htm) contains the information about the EU Clinical Trials Directive [2001/20/EC], trial authorisation and a helpful FAQ page.

Consumer involvement in research

The HTA programme recognises the increasing active involvement of consumers in research and would like to support research projects appropriately. The HTA programme encourages applicants to include the active and full participation of consumer involvement in the proposed proposal development.

Communication

Successful applicants will be required to submit a single final document in the form of a full proposal to the HTA programme.

Timescale and Costs

A short two page word document briefly summarising the work needed to develop a full proposal, together with proposed costs is required. This should be emailed to Pauline Swinburne, External Projects Manager (Pauline@soton.ac.uk) no later than the 24th February 2005. Once received, this will be reviewed internally and the applicant notified early in March 2005 (subject to our satisfaction) of our agreement to commission. Whilst it is difficult to set boundaries, as a guideline, previous proposal development projects funded by the HTA programme have not exceeded £30,000. The successful applicant must be aware that **the delivery date of the full proposal is no later than 31st May 2005.**