# Ultrasonography in the diagnosis of Giant-Cell Arteritis (GCA)

## 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, provide care in or develop policy for the NHS. Topics for research are identified and prioritised to meet the needs of the NHS. Health technology assessment forms a substantial portfolio of work within the National Institute for Health Research and each year about fifty new studies are commissioned to help answer questions of direct importance to the NHS. The studies include both primary research and evidence synthesis.

## Question

***What is the added value of high resolution ultrasonography in the diagnosis of GCA? Can it be used to triage patients suspected of GCA and predict those who need or don't need a biopsy?***

1 **Technology:** High resolution ultrasonography.
2 **Patient group:** Patients suspected with a moderate to high risk of GCA assessed as appropriate for temporal artery biopsy.
3 **Setting:** Any.
4 **Control or comparator treatment:** Reference standard is biopsy and histology (or to be specified by researcher).
5 **Design:** Primary research; a diagnostic accuracy study to compare the performance, costs (including the costs of the consequences of missed diagnosis) and acceptability of ultrasonography in the diagnosis GCA. The findings of this research should identify the most effective test order and/or combination of tests, such as determining the added value of biopsy or ultrasonography (or both, and in what order) after utilizing the American College of Rheumatology (ACR) criteria tool.
6 **Primary outcomes:** Diagnostic accuracy, sensitivity/specificity. Secondary outcomes: a diagnostic algorithm, changes in patient management and resource use, cost-effectiveness; patient preference and adverse events.
7 **Minimum duration of follow-up:** 6 months (alternative durations should be justified).

### Background to commissioning brief:

*Giant cell arteritis (GCA) is a relatively common form of systemic vasculitis. Prompt diagnosis and treatment are important to prevent serious vascular complications, particularly visual loss. Serious complications include facial nerve damage, infection, skin necrosis, and stroke. Biopsy results may be negative in 9% to 44% of patients with a clinical diagnosis of GCA. In Scandinavia and northern Europe the incidence has been reported as 6-18 per 100,000 people over the age of 50. The American College of Rheumatology (ACR) has proposed diagnostic criteria for GCA based on history, physical examination, and laboratory and biopsy findings. Three of the five criteria must be met for patients to be classified as having GCA.*

*The reference standard remains temporal artery biopsy, followed by treatment with corticosteroids. To avoid a false negative biopsy, excision of up to 3cm of the artery has been recommended, thereby increasing morbidity, and potentially leading patients to refuse the procedure. For patients who refuse biopsy, ultrasonography has been used for diagnosis.*

## Notes to Applicants

For many of the questions posed by the HTA programme, a randomised controlled trial is likely to be the most appropriate method of providing an answer. However, there may be practical or ethical reasons why this might not be possible. Applicants proposing other research methods are invited to justify these choices.

Applicants are asked to:

1. 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. Further advice specific to each topic will be given by the HTA programme at full proposal and contract stages.

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 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 reserve 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. The DH/MRC website (http://www.ct-toolkit.ac.uk/) also contains the latest information about Clinical Trials regulations and a helpful FAQ page.

## Research networks

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

## Making an application

If you wish to submit an outline proposal on this topic, complete the electronic application form and return it to the HTA Commissioning Manager at the National Coordinating Centre for Health Technology Assessment, Mailpoint 728 Boldrewood, University of Southampton, Southampton SO16 7PX by **{date}.** Outline applications will be considered by the HTA Commissioning Board at its meeting in **November, 2008**. If they are 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.***

***Please see GUIDANCE ON APPLICATIONS overleaf.***

## Guidance on applications

**Required expertise**

HTA is a multidisciplinary enterprise. It needs 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. The HTA programme expects teams proposing randomised controlled trials to include input from an accredited clinical trials unit, or one with equivalent experience. Applicants are also expected to engage a qualified Trial Manager for appropriate projects. A commitment to team working must be shown and applicants may wish to consider a collaborative approach between several institutions.

**Public involvement in research**

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.

**Outcomes**

Wherever possible, the results of HTA should provide information about the effectiveness and cost-effectiveness of care provided in its usual clinical setting and for the diverse subjects who would be eligible for the interventions under study. The endpoints of interest will in most cases include disease specific measures, health related quality of life and costs (directly and indirectly related to patient management). Wherever possible, these measurements should be made by individuals who are unaware of the treatment allocation of the subjects they are assessing. We encourage applicants to involve users of health care in the preparation of their proposal, for instance in selecting patient-oriented outcomes. A period of follow up should be undertaken which is sufficient to ensure that a wider range of effects are identified other than those which are evident immediately after treatment. These factors should guide applicants in their choice of subjects, settings and measurements made.

**Sample size**

A formal estimate should be made of the number of subjects required to show important differences in the chosen primary outcome measure. Justification of this estimate will be expected in the application.

**Communication**

Communication of the results of research to decision makers in the NHS is central to the HTA Programme. Successful applicants will be required to submit a single final report for publication by the HTA programme. They are also required to seek peer-reviewed publication of their results elsewhere and may also be asked to support the NCCHTA in further efforts to ensure that results are readily available to all relevant parties in the NHS. Where findings demonstrate continuing uncertainty, these should be highlighted as areas for further research.

**Timescale**

There are no fixed limits on the duration of projects or funding and proposals should be tailored to fully address the problem (including long-term follow-up if necessary). Applicants should consider however that there is a pressing need within the NHS for this research, and so the duration of the research needs to be timely.

In evaluating diagnostic and imaging techniques, the emphasis of the HTA programme is to assess the effect on patient management and outcomes (particularly where changes in management can be shown to have patient benefits). Improvements in diagnostic accuracy, whilst relevant, are not the primary interest of this commissioned research programme. Applicants should justify where they consider improvements in diagnostic accuracy to be relevant to these objectives. Where there is poor evidence to link diagnostic improvements to patient benefits, part of the primary research may be to assess the effects of such changes on patient outcome.

An assessment should also be made of changes in other resources (particularly other subsequent therapies) used as a result of changes in diagnostic methods.