

Understanding the Mechanisms of CFS/ME: Guidance for Panel Members

As you know, MRC has issued a £1.5M call for proposals, Understanding the Mechanisms of CFS/ME. Thank you for agreeing to assist in prioritising these proposals for funding. You have been assigned to 'introduce' certain applications (these assignments can be found on the Panel Agenda), but we ask that you read and be prepared to comment on all of the proposals to ensure a comprehensive Panel discussion.

This document provides guidance to help you in your assessment of these proposals, particularly:

- the [context](#) around this call for proposals;
- the [focus of the call](#);
- the various [documents](#) which the applicants were required to submit, particularly the [Case for Support](#);
- the [criteria](#) you should consider in your assessment of the proposal.

Context

Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) is a complex and serious debilitating medical condition with a diverse range of symptoms. Profound physical and/or mental fatigue is the most well-known, while others include pain, disturbed sleep patterns and gastrointestinal problems. Each patient experiences their own personal combination of symptoms.

CFS/ME research has been a [high priority area for the MRC](#) for some time. The development of this call for proposals has been informed by the work of the [MRC Expert Group](#), (chaired by Professor Stephen Holgate), other experts in the field of CFS/ME and research leaders in aligned areas who have identified and prioritised medical research topics where the MRC might target efforts to encourage and support high-quality proposals.

Focus of the call

CFS/ME is a complex, heterogeneous condition that comprises the interaction of different biological, physical and psychological mechanisms. Understanding these mechanistic pathways and the interactions between them is important in improving understanding of the condition.

The focus of this initiative is to support high-quality, innovative medical research that increases the current knowledge base of CFS/ME; and on drawing in expertise and resources from related research fields. Applications must address the mechanisms underlying chronic changes related to CFS/ME, particularly focusing on one or more of the following areas:

Autonomic dysfunction: In CFS/ME evidence supports an association between the condition and various forms of hypotension, reduced heart rate variability, alterations in the hypothalamic-pituitary-adrenal axis and sympathetic stress response systems.

Cognitive symptoms: Cognitive problems are commonly reported in CFS/ME. These include impaired short-term working memory and thinking, difficulties with concentration and attention span, and impaired information processing.

Fatigue: Chronic disabling fatigue is a common, poorly understood phenomenon. There is a need to better understand the measurement and mechanisms of central (brain) and peripheral (muscle) fatigue and post-exertional malaise as well as the influence of complicating factors such as depression, sleep disorders and pain.

Immune dysregulation: There is evidence for a disturbance in innate and adaptive immunity in CFS/ME including alterations in cytokine profile, absolute and functional alterations in T cells and NK cells and occurrence of autoantibodies and allergic reactions that may explain some of the manifestations such as fatigue and flu-like symptoms. A number of infectious and environmental exposures have been associated as triggering these changes.

Pain: Headache, facial pain and myalgia are reported symptoms of CFS/ME that may involve altered sensory and/or cognitive processing in the relevant neural pathways.

Sleep disorders: Disordered sleep is a characteristic symptom in CFS/ME including, impaired daily sleep/wake rhythms and disrupted sleep,

hypersomnia, insomnia, and secondary problems such as restless legs syndrome.

Applications should seek to understand these mechanisms through the study of cross-disease symptomology, and pathways, in the clinic and/or laboratory. Additionally, this initiative aims to address the current lack of capacity in CFS/ME research, and the need for multidisciplinary teams to tackle the significant research challenges in this area. Proposals submitted to this call must therefore involve partnerships between CFS/ME researchers and established, leading investigators working in relevant areas, but who are new to the CFS/ME field. It is expected that those investigators who are new to CFS/ME research will make a substantial contribution to the programme of work, to enable them to build their own track record in CFS/ME research. The capacity building aspect of the call is focused on bringing new established investigators into CFS/ME research; therefore, applicants may not request PhD studentships as part of this call.

Proposal Documents

Applicants were required to submit the following documentation:

- A Case for Support – further guidance on what is expected in the case for support can be found below;
- A CV and list of recent publications for each named researcher;
- A statement justifying the resources requested for the project – this attachment is known as the Justification of Resources;
- A Pathways to Impact Statement – guidance from MRC on assessment of impact can be found at:
<http://www.mrc.ac.uk/Fundingopportunities/Applicanhandbook/PathwaystoImpact/index.htm> (particularly under the 'Assessment' heading).

Additionally, some applications may contain Letters of Support from project partners.

Each application will also contain peer review comments and the applicants' response to these comments (see 'Application Assessment' below for further information).

Please read all documents related to each application.

Case for support

Applicants were required to prepare a case for support (maximum 8 pages A4) as part of their application.

The case for support should contain the following sections, if appropriate:

1. Title
2. Importance of the research
3. Scientific potential
 - 3.1 People and track record – this section should include details of which investigator(s) are new to CFS/ME research and how their expertise is relevant to research in this area.
 - 3.2 Research environment
 - 3.3 Research plans – in addition to detailed research plans, this section should outline the investigators' approach to their partnership and clearly indicate which investigator(s) will carry out each aspect of the proposed programme of work.
4. Ethics and research governance
5. Data preservation for sharing
6. Dissemination - plans for dissemination to potential academic beneficiaries should be included here; details of plans for public engagement, exploitation of results and/or dissemination to potential non-academic beneficiaries should be included in the Pathways to Impact statement.

Application assessment

Each application has been sent out to peer-reviewers with the aim of securing comments covering all aspects of the proposed work. These peer-review comments have been provided to the applicants and they have been given the chance to respond to them. Please read all reviewers' comments and the applicants' response as part of your assessment of the proposals.

In assessing this application, please use the following criteria:

- Research quality;
- Impact - importance, innovation and timeliness of the research and its likely contribution to the CFS/ME research knowledge base;
- Productivity;
- Fit to the call:

- Does the proposed work address one or more of the identified priority research areas?
- Does the investigator group include one or more researchers who are new to CFS/ME research? Do they have the appropriate skills and expertise to make a positive contribution to the CFS/ME research base in the UK? Is the partnership likely to help build capacity in CFS/ME research in the UK?

At the Panel Meeting, each proposal will be discussed in turn. Each Panel Member will be asked to provide a score (1-10) for the proposal taking into account reviewer reports, the applicant's response and their own judgement. Indicators for each score can be found in the Reviewers' Handbook Extract (included on the Panel FTP site, page 60-61). This score will be used to help rank proposals and will be made know to applicants. After all proposals have been discussed and the rank-ordered list has been generated, there will be time for further discussion to finalise the list and make funding recommendations.

The Panel's recommendations for funding will be presented to the MRC Population and Systems Medicine Board at their Meeting on 16-17 November 2011 for ratification.