Response from the National Patient Safety Agency to Complaint about the PACE Trial

Margaret Williams

14th April 2010

Updated 2 Feb 2018 to include a facsimile of the full response as an addendum to the article

On 1st March 2010 Professor Malcolm Hooper lodged a complaint with the Head of the National Research Ethics Service (NRES) – formerly the Central Office for Research Ethics Committees (COREC) which on 1st April 2007 became NRES -- about the apparent failure of the West Midlands Multicentre Research Ethics Committee (West Midlands MREC) to fulfil its obligations before granting ethical approval for the MRC PACE Trial on the grounds that it failed to adhere to Section 9.7 of the Governance arrangements for NHS Research Ethics Committees (2001) which were in place at the time it granted ethical approval for the MRC PACE Trial.

The complaint set out numerous heads of concern and concluded:

"It seems indisputable that, either through dereliction of duty or through being inadequately informed by the Chief Investigator, the West Midlands MREC failed to adhere to section 9.7 of the Governance arrangements for NHS Research Ethics Committees (2001) which were in place at the time it granted ethical approval for the MRC Trial**.**

Given the nature of these ethical concerns, there should be serious consideration given to the continuation of the Trial and the publication of any data".

The full complaint can be accessed at http://margaretwilliams.me/2010/mrec-complaint.pdf

Response

On 22nd March 2010 a response was sent by Dr Janet Wisely, Director of the National Research Ethics Services, which is part of the National Patient Safety Agency, 4-8 Maple Street, London W1T 5HD.

The full response is given below.

Extracts from the response include the following:

"In the case of the PACE Trial I have concluded that there is no likely benefit of a more extensive review of the original decision made by the REC because it was a decision made a long time ago".

"The REC does have a role after the original approval, however it has no power to investigate".

"Where the REC has concerns that there may be issues of misconduct then again it has no powers to investigate".

"In the case of PACE the study is closed for new recruitment and I do not think it appropriate to ask the REC to reconsider the opinion that was made several years ago. What NRES is able to do is to pass on the concerns that have been raised to those with responsibility for the conduct of the trail (sic) for their consideration. However, it seems there has been extensive dialogue with these relevant parties and I do not feel there is anything that NRES can usefully add to these exchanges".

Given the expressed concerns about patient safety, particularly in the graded exercise arm of the PACE Trial, the response is considered unsatisfactory.

Please scroll down to see the full response

National Patient Safety Agency

Our Ref: JW/619/sr

Malcolm Hooper
Emeritus Professor of Medicinal Chemistry
University of Sunderland
Edingburgh Gateway
Chester Road, Sunderland,
Tyne and Wear
SR1 3SD

National Patient Safety Agency
4-8 Maple Street
London W1T 5HD

Tel: 020 7927 9898
Fax: 020 7927 9899
queries@nres.npsa.nhs.uk
www.nres.npsa.nhs.uk

22 March 2010

Dear Professor Hooper

Thank you for your letter and enclosures regarding the PACE trial which I have now had opportunity to consider. We have also requested confirmation from the Chief Investigator of the status of the study who has confirmed that the study has closed for recruitment of new participants. I consider the main issues, from the perspective of the ethical review and role of NRES, as the original ethical opinion and the ongoing management and conduct of the trial. I have replied below to these separate issues.

The original ethical opinion

A REC makes an independent ethical decision within a framework, which at the time of this decision was provided and managed by what was COREC (Central Office for Research Ethics Committees) which had responsibility for the Multi centre Research Ethics Committees. GAfREC (Governance Arrangements for Research Ethics Committees) describes the governance arrangements for ethics committees, including a framework for the ethical considerations.

The management of ethical review has changed considerably in the UK, largely on the back of the Clinical Trials Regulations and other legislation that mean RECs are increasingly making an independent ethical decision within a legal framework. All RECs now work to NRES standard operating procedures (SOPs), which are available on the NRES website and Governance Arrangements continue to be described by Department of Health in GAfREC.

The principles behind the ethical review remain unchanged, the decision is independent. The REC is guided to consider ethical issues described in guidance and guidelines but ultimately they make an independent decision on a collective discussion and review of the information provided and required as described in our standard procedures. With the exception of some specific elements of more recent legislation such as the Mental Capacity Act, which makes particular requirements that may enable a determination that a REC has made an 'incorrect decision', the legislation governing REC review provides a framework for the decision making but does not prescribe the decision that should be reached.

An applicant may appeal against a decision made by a REC, and procedures are described for an appeal to be heard by another committee. There is no appeal procedure for others against a decision made by a REC. Ultimately participants are consenting to enter a trial, or not, based on the protocol and information approved by the REC. On rare occasions where we receive a complaint or concerns about a REC decision we may review the decision to inform a response or for learning points. The decision of the REC cannot be changed by anyone other than the REC reviewing the decision again in the light of new available information. In the case of the PACE trial I have concluded that there is no likely benefit of a more extensive review of the original decision made by the REC, because it was a decision made a long time ago which is unlikely therefore to reveal relevant learning points for NRES, and importantly and specifically because the study is closed to new recruitment.

Research conduct and management of the trial

The REC does have a role after the original approval, however it has no power to investigate. The REC role is to review information that is made available to it by the Chief Investigator and Sponsor. for examples as is provided via amendments or routine study reports. A REC may consider again the ethical opinion at a quorate meeting of the REC and may reconsider if it still has a favourable ethical opinion: the REC options being to terminate or suspend the ethical opinion. For Clinical Trials under the Clinical Trials Regulations the decision to suspend lies with the MHRA, and in this case the REC would raise any concerns through the MHRA.

Where the REC has concerns that there may be issues of misconduct then again it has no powers to investigate. Procedures are described within our SOPs by which NRES will raise the concerns with those responsible for the conduct of the trial, the Sponsor, and the REC appointing authority.

In the case of PACE the study is closed for new recruitment and I do not think it appropriate therefore to ask the REC to reconsider the opinion that was made several years ago. What NRES is able to do is to pass on the concerns that have been raised to those with responsibility for the conduct of the trail for their consideration. However, it seems from the correspondence provided that there has been extensive dialogue and exchanges with these relevant parties and I do not feel there is anything that NRES can usefully add to these exchanges.

I am sorry I cannot be more helpful on this occasion, I hope this letter goes some way to describe the remit of the REC and NRES with respect to the framework for the independent review and the NRES procedures in place for referring on suspected cases of misconduct.

Yours sincerely

Janet Wisely

Dr Janet Wisely
Director
National Research Ethics Service (NRES)