PACE Trial

Trial Management Group Meeting # 9

Thursday 8th July 2004

1. Those present

[redacted]

2. Apologies were received from

[redacted]

3. Previous minutes for TMG #7

a) Corrections and amendments to Minutes TMG #7 –

- Correction to spelling of [redacted] name.
- Add [redacted] to people present.
- Amend item 13 to read 'A SOP will need to be written to cover protocol deviations and obviously will need to *be defined in the analysis strategy*.'

- Amend item 19(i) to read 'We would then be able to determine the percentage of people who improve on either symptoms or disability or both measures.'

- Amend item 25 to change 'sort' to 'sought'.

b) Item 5 Action point to be reiterated in these minutes:

ACTION: Centre leaders to ensure all LREC, R&D, Caldicott Guardian and Data Protection approvals are in place.

c) Item 10 Action point to be reiterated in these minutes:

ACTION: [redacted] to sort out NHS support costs for doctors with [redacted].

ACTION: [redacted] to write SOP to define 'changes from randomised treatment' with the assistance of [redacted] and [redacted] in order to distinguish participants who withdraw from treatment from those who are lost to follow-up.

d) **TSC and DMEC.** [redacted] are to join the TSC, and [redacted] has agreed to Chair the DMEC. [redacted] appointment will need to be approved by the MRC and TSC.

ACTION: [redacted] to contact the MRC for approval for [redacted] *This obtained 11/07/2004.*

ACTION: [redacted] to alert [redacted] to the date of the joint TSC/DMEC meeting in anticipation of his formal approval as DMEC Chair*. Done 13.7.04*

e) **Sponsorship.** Clarification that Queen Mary has agreed to be the main sponsor for the PACE Trial but sponsorship will also need to be delegated at a local level.

ACTION: All Centre leaders to clarify local sponsorship and associated indemnity. Correspondence relating to this should be copied to [redacted]

f) **Objective measures of outcome.** This still in discussion from last meeting.

ACTION: [redacted] to contact [redacted] to check this.

g) **Audio recording of therapy sessions.** £20,253 has been assigned for rating the audiotapes. The tapes serve four main purposes (i) to judge therapist competency, (ii) to assess therapeutic integrity, (iii) to ensure that the therapies are differentiated and (iv) for supervisory feedback.

ACTION: [redacted] to investigate who should independently assess the tapes.

ACTION: [redacted] to ensure that the PIS and consent form state that the audio recordings may be kept for twenty years (in keeping with MRC practice for retention of source materials).

ACTION: [redacted] to make a decision on the use of digital audio recording equipment, following demonstration of same in Edinburgh.

ACTION: [redacted] to investigate video teleconferencing facilities at Barts.

4. Previous minutes for TMG #8

a) Corrections and amendments to Minutes TMG #8 –

Item 6; change 'six months' to 'three months'

Item 13, Summary of agreed point, point 2; delete the words 'measure bias'.

b) **Medical screening.**

ACTION: [redacted] to complete SOP for recording all new clinic patients, and their eligibility/non-eligibility.

c) Patient Information Sheets and Leaflets. Two possibilities have emerged for re-writing the Patient Information documents in lay terms. The first option comes via [redacted] who has been contacted by a patient who will write information sheets in lay language at no cost. The second option is [redacted], an editor who has experience of writing similar documents for other MRC trials and is available to help with PACE. [redacted] charge is at £25 per hour (half price as we are public sector) and recommends that we supply [redacted] with details of the documents (word count, number of leaflets) and an upper estimate of how much we are able to spend.

ACTION: [redacted] to define which documents require this treatment and contact [redacted] for a further quote.

ACTION: [redacted] to ensure that the PIS and consent form includes both information recorded on paper and electronically.

d) Item 10 Action point 4 to be reiterated in these minutes:

ACTION: [redacted] to check that the following is covered in the PIS and consent form. 'I agree not to be referred to another therapist through the duration of my involvement in the trial?'

e) Item 13 Action point 1 to be reiterated in these minutes (note the slight change of wording from 'should' to 'might'):

ACTION: [redacted] to design this question proforma/CRF. Patients in each arm of the trial should be asked the following questions at four time points (Baseline, 10 weeks, 6 months and 12 months):

Qualitatively: 'What do you think you might do in order to get better?

What are you doing?'

Quantitatively: 'Are you a) pushing the envelope, b) working within it'

f) **SSMC leader.** [redacted] has kindly agreed to take on this role.

g) **PACE e-mail address.** The PACE trial e-mail address has been set-up: pace@qmul.ac.uk. [redacted] and [redacted] both have access to read and respond to these. This email address can be passed on to those who wish to contact the lead/administrative centre, which may be useful if you do not wish to pass on named email addresses or if there is a general enquiry.

5. **Economic costs.** [redacted] gave a brief summary of a recently published paper that had been circulated previously.

   Reynolds, K.J., Vernon, S.D., Bouchery, E., Reeves, W.C. (2004), The economic impact of chronic fatigue syndrome. Cost effectiveness and Resource Allocation 2:4

6. **Discussion about papers circulated.** Regarding the Moss-Morris GET RCT, it was notable that self-efficacy was a predictor and that symptom focussing mediated change with GET.

   Moss-Morris, R., Wash, C., Tobin, R., Baldi, J.C. (2004) A Randomised Controlled Graded Exercise Trial for Chronic Fatigue Syndrome: Outcomes and Mechanisms of Change. In press.

7. **Standardised Specialist Medical Care (SSMC)**

   ACTION: [redacted] to think further about process of SSMC to ensure that it is consistent between both all four arms and all six centres.

   ACTION: [redacted] to consider the changes proposed by [redacted] to the Clinic Information Leaflet, and then circulate the final version to [redacted] and finally [redacted].

   ACTION: [redacted] to delete SSMC from the three supplementary treatments in the clinic leaflet.

   ACTION: [redacted] to write a standardised letter to go to the patient prior to the first clinic appointment.

8. **Protocol development.**

ACTION: [redacted] to make alterations to the protocol as discussed in the meeting.

ACTION: PIs to discuss the following: The suggestion was made to explicitly state conditions that would be exclusions to the trial, as covered by the Oxford criteria. Since the Oxford Criteria are not that explicit, this needs further thought.

ACTION: [redacted] **to visit** [redacted] to discuss review of protocol layout and order of sections

ACTION: [redacted] **and** [redacted] to ensure that the hypotheses are in the Analysis Strategy document

ACTION: [redacted] to check with [redacted] whether ancillary studies require TSC approval.

ACTION: [redacted] to clarify participant pathway once referred to the RN. (i) Initial screening telephone call with RN, (ii) first visit, consent, actigraphy, (iii) return with actometer, and randomise.

ACTION: [redacted] to address issues of screening and eligibility (up to section 6.3 in protocol).

ACTION: [redacted] to decide whether to use ICD10 or DSMIV for depressive disorder for minimization.

ACTION: [redacted] to ensure that the database does not include information on which treatment the participants have been allocated to.

ACTION: [redacted] to ensure that minimisation within centres is balanced to avoid long runs of randomisations assigning participants all to the same therapist.

ACTION: [redacted] to write SOP for assessing plausibility of therapy.

ACTION: [redacted] to check with [redacted] regarding other alterations to be made to Section 10.

ACTION: [redacted] to write SOPs for quality assurance (QA) and quality control (QC).

ACTION: [redacted] to advise on alterations to section 19, Publications.

ACTION: [redacted] to ensure that indemnity is clarified in the protocol.

Move to protocol ACTION: Oxford PIs to identify their local medical expert.

9. **Source notes.**

ACTION: [redacted] to write an SOP to describe (i) what information should go into the clinical notes about the trial, (ii) what clinical information should go into the trial specific source notes, (iii) whether a sticker can and should be attached to the front of the clinical notes alerting the fact that the patient is in the trial and that the notes must not be destroyed, and (iv) what can and cannot be put in the notes.

10. **SAEs and SARs.** Serious adverse events and adverse reactions will be reported to the appropriate committees in times suggested by EU guidelines for Good Clinical Practice for clinical trials although it was noted that as it is a non-pharmacological trial, PACE is not obliged to abide by these regulations.

11. **Information sheets and leaflets (PIS & PIL).** It was noted that the descriptions of the therapies should be consistent across all trial documentation and tools.

    ACTION: All therapy leaders ([redacted] to e-mail [redacted] with a new version of the description of their own specialist therapy.

    ACTION: [redacted] to ensure these are slotted into the appropriate documents and circulated to the therapy leaders for inclusion in their manuals.

    ACTION: [redacted] to re-name Patient Information Sheet to Participant Information Sheet and complete all suggested changes to this document:

    - add information that data will be stored for twenty years (including audio recordings)
    - include information relating to the study stopping.

    ACTION: [redacted] to review the section relating to pregnancy. [redacted] incorporate any changes decided upon.

    ACTION: [redacted] to ask QMUL legal department to review the PIS.

12. Predictors of response.

    ACTION: [redacted] to add self-efficacy, age and 'in dispute or negotiation of benefits' to section 10.1.

    ACTION: [redacted] to look at self-efficacy measures.

13. **Equipment.**

    ACTION: [redacted] to add scales and tape measures (for height and weight calculations) to the equipment list.

14. Exclusion of somatisation disorder

ACTION: [redacted] [redacted] [redacted] to discuss and recommend exclusion of somatisation disorder or exclusion of patients who would not benefit from being in the trial.

15. **CSRI**

ACTION: [redacted] to add Occupational therapy, and negotiation of medical retirement to the CSRI.

16. **Database.**

ACTION: [redacted] to complete CRF design so that database may be written (to be completed once protocol finalised).

ACTION: [redacted] to write database in Access.

17. **GET Manual.**

It was noted that there were concerns that the manual contained too much information relating to sleep, although it was argued that it was important to include advice on this in the therapy, since it was consistent with advice of relevance to a GET programme.

ACTION: [redacted] to include appropriate advice and education about sleep in the GET manual consistent with that given by a specialist physiotherapist. And to ensure that information relating to SSMC is added in (missing from page 11).

18. CBT Manual

It was noted that CBT could include discussion of physical exercise, consistent with advice that a specialist CBT therapist would give.

19. **SSMC**

ACTION: [redacted] to add in to protocol that non-benzodiazepine hypnotics are not allowed as they may interfere with therapies.

20. **Schedule for start.**

ACTION: [redacted] to produce a project schedule.

21. Budget Costs

We agreed that the travel and consumables budgets will be allocated with 25% monies removed to provide a contingency pot for the future.

22. **Date of next meeting.** 1pm to 5pm, Wednesday, 15th September 2004 in the [redacted]

[redacted]