1.30pm – 5 pm, Wednesday 29th June 2005

[redacted]

PACE Trial Steering Committee
Draft Minutes

1. Those present and apologies

Independent members

[redacted]

Other members

[redacted]

Observers

[redacted]

Apologies

[redacted]

2. DMEC report

The DMEC will produce a formal report. The following is based on the initial verbal feedback from the chair [redacted]

a) Definition of deterioration

The DMEC needs to have a definition of serious deterioration in order to monitor possible deleterious effects of the therapies within the trial and asked the TMG to develop one. The measures suggested as part of a definition of serious deterioration might include a combination of:-

- Step test – for an objective measure
- HADS – depression
- PHQ-15 physical symptoms questionnaire – subjective measure

The normal distribution of the scores for these scales would be helpful in order to define serious deterioration. . It was suggested that participant *drop out rates* by treatment could be a good proxy for identifying potential problems but that it would be important to consider the individual reasons for drop out and not just look at the numbers. The TSC suggested that the TMG might also consider a measure of *life participation* as people might be able to maintain therapy but social/work functioning might be reduced.

Further discussion led to a recommendation that a combination of both drop-out and self report by treatment should be considered. Self-rated global deterioration could be used as a possible single measure but it might be preferable to have more than one.

ACTION 1: The PIs in conjunction with [redacted] to respond to the DMEC request to develop an operational definition of serious deterioration. This definition should be sent to the DMEC & TSC for comment by email rather than wait for next meeting.

b) Life participation

The DMEC noted that participation in activities is not directly measured. They accept that a new questionnaire would add to burden and suggested that the PIs identify items within other questionnaires that might be used to measure this. (This might also form part of the definition of serious deterioration – see above)

ACTION 2: PI's with help of the statisticians and DMEC, to consider how best to measure life participation.

c) Frequency of meetings

The DMEC would plan to meet annually to consider the data and preferably one month before the TSC in order to allow enough time to produce a report for consideration by the TSC.

ACTION 3: [redacted] to set up dates for next year's meetings for the TSC and DMEC.

d) Recruitment of participants

The DMEC would like a recruitment report every 6 months.

ACTION 4: [redacted] to send the DMEC recruitment reports annually.

e) Participation in therapy

The DMEC were interested in receiving data about any lack of attendance at treatment sessions and would like to know what is happening on a per session basis. The DMEC requested annual reports on this.

ACTION 5: PI's to address how participant attendance might be recorded on a session by session basis and the format of the report for DMEC.

f) Participant follow-up

The DMEC noted that it might be possible for patients to attend therapy but not attend for outcome assessment and asked whether the PIs had considered this. The PIs reported that so far there have been no cases of participants missing outcome assessments but they would monitor this carefully

ACTION 6: PIs to monitor attendance to therapy versus attendance to follow-up visits.

g) Competing research

The DMEC and TSC would both like a summary table from the PIs at each meeting that provided an update on all other relevant ongoing and published research into CFS/ME.

ACTION 7: PI's to provide a summary report for each meeting listing all ongoing research and recent publications.

3. Agreement of agenda

The agenda for the meeting was agreed by all.

4. Previous minutes of TSC # 2

The previous minutes were agreed apart from one change to page 5 detailing the rationale for the choice of criteria for PACE.

ACTION 8: [redacted] to send a revised paragraph to [redacted] for incorporation into the final draft of the minutes for TSC meeting #2.

a) Indemnity

It was reported that since the last meeting it has been confirmed that the sponsor (Queen Mary University of London) is responsible for indemnity and that the MRC do not provide indemnity for studies that they fund but are not the sponsor.

b) Adverse experiences of randomisation to SSMC

The PIs reported that they are aware of two participants for whom the experience of being randomised to SSMC alone was associated with increased distress. However, the first of these participants has been seen for a follow up assessment with the research nurse and reported only transient low mood which the participant does not attribute to the randomisation. The second participant is being closely monitored with nothing to report so far. It was also noted that conversely some participants have refused PACE on the grounds that they would prefer to receive SSMC alone and did not wish to take the chance of being randomised to one of the therapies.

c) Meeting documentation

The TSC requested that at future meetings the supplementary documents are numbered according to their place on the agenda for easier reference.

ACTION 9: [redacted] for future meetings, to number the papers according to their place on the Agenda.

5. Recruitment update

a) Start date of recruitment

[redacted] presented a recruitment report to the TSC. It was noted that the trial was delayed in starting recruitment due to delays with the MREC approval of trial amendments. When allowing for the delay, recruitment was at 95% of target at the end of May and at slightly over 100% at the time of the TMG (31 participants recruited; target=30).

The TSC would like to review the screening and recruitment data but will remain blind to the numbers allocated to each treatment option.

b) Proposed end date for recruitment

Currently, the end date for recruitment has been revised and is two weeks later than originally proposed in the protocol to allow time to catch up on the three month delay to the start of recruitment. The TSC would like to be kept informed how feasible this end date is within the limitations of the grant and the PIs assured the TSC that this would be carefully monitored.

c) Actual recruitment versus target recruitment by centre

All the three lead centres have opened and recruited at a similar rate. The TSC request that the TMG review relative recruitment rates at each meeting and alert the TSC if there is a problem with recruitment at any centre(s).

ACTION 10: TMG to review data on recruitment by centre at each meeting and alert the TSC immediately if there is a problem with recruitment at any centre(s).

The TSC asked if the PIs saw any future potential problems that might threaten recruitment to the trial. The PIs have considered whether the opening of fifty new CFS centres might take patients away from PACE. However it is felt that if this happened, the TMG could explore the possibility of recruiting to the trial from these centres.

d) Acceptance rate as a proportion of those offered the trial

It was explained that at present it appears as though there is a large difference between the number of participants screened and those offered and accepting the trial. The TMG members offered the following explanations for this:

i. Screening takes place at two stages: Patients are screened at the secondary care clinic by the clinic doctors for their suitability for the PACE trial. If thought suitable they are referred to the research nurse. Secondly, referred patients are screened at the baseline 1 visit for the trial. Suitable patients are randomised at the baseline 2 visit.

ii. NHS activity complicates this diagram because it can take some time for a patient's diagnosis to be confirmed. The CONSORT diagram presented includes all patients referred to one of the participating secondary care clinics with a suspected diagnosis of CFS/ME. Once these patients have been assessed by a clinic doctor, other reasons for their CFS may emerge (e.g. hepatitis, thyroid problems etc). In order to confirm a diagnosis it may be necessary to refer the patient for other investigations in other clinics first. The screening figures presented do not differentiate between those participants referred with a suspected diagnosis of CFS/ME and those who go on to have this diagnosis confirmed.

iii. There are a proportion of participants (17) who have been offered the trial subject to blood results being obtained to confirm diagnosis and eligibility.

iv. Therefore, the largest proportion of patients that appear as screen failures are those either definitely screened out by the clinic doctors, or those awaiting confirmation of diagnosis or those awaiting blood results. Only a very small portion of patients fail at the baseline 1 screening stage (i.e. after diagnosis and blood results are known).

The TSC were satisfied with these explanations and ask that the data on the numbers screened and who decline is given in greater detail at future meetings. The TSC also asked the TMG to monitor this.

ACTION 11: [redacted] to present extra information in future reports showing the proportion of participants whose diagnosis of CFS/ME is confirmed of those referred to the clinic.

ACTION 12: [redacted] to alter the word 'refuse' to 'decline' on the CONSORT diagram.

ACTION 13: [redacted] to add a line in to the CONSORT diagram to show Acceptance Rates as % of Eligible.

ACTION 14: [redacted] to review the group who declined in greater detail and report any problems to the TSC

e) Forecasts for recruitment

[redacted] presented a revised recruitment chart for the trial to take into account the delay to starting. At this time, the target end date for recruitment has been delayed by two weeks.

f) Drop out, withdrawals and losses to follow up by month and as a proportion of those entered

Drop outs are classified as those participants who opt to withdraw from the trial or who are withdrawn from the trial by the PI/centre leader. Losses to follow-up are those participants who do not attend follow up sessions and give no reasons for their withdrawal from the trial.

There are no reported drop outs or losses to follow up at this time.

g) Serious adverse events and reactions

Additionally there have been no serious adverse events or severe reactions reported.

h) Completeness of data

The trial database is almost complete and ready to distribute to centres to begin data entry. For this reason, no data entry has yet taken place and missing data cannot be reported at this time. The TSC requested a report on completeness of data at future meetings and commented that the TMG should monitor completeness of data at every meeting.

ACTION 15: [redacted] to inform the DMEC and TSC if there are any concerns regarding completeness of data.

i) Relevant published studies since last meeting (e.g. Ross-Morris and Wallman GET studies and Adolescent CBT study)

For future meetings, the DMEC and TSC would like a summary report presented which details:

- All other ongoing and published research into CFS/ME
- A summary of what (if any) impact this will have on PACE; for example, are the estimated effect sizes likely to be different to that which we expect?

It was agreed that the new papers presented to the TSC are not likely to have an impact on PACE. The PIs are aware of another trial that is closing shortly and due to be analysed in the near future.

It was noted by the TSC that rates of participants 'lost to follow-up' were high in the presented papers. It was felt likely that this was in part due to the use of intrusive measures such as gas analysis.

ACTION 16: PI's to summarise all other studies going on in the area of CFS/ME which should include outcome data and the numbers of participants included. This will include the conclusions of a meta-analysis.

j) Summary of other discussions

At each future meeting, the TSC should review:

- Actual vs. target recruitment
- Acceptance rate
- Loss to follow-up
- Adherence to treatment
- Baseline data but not outcome data.
- A report on data quality (the DMEC will also review this)

ACTION 17: [redacted] to present the same report to TSC as to DMEC but the data will not be presented by treatment group.

ACTION 18: [redacted] and the PIs to develop the format for this report to show to DMEC and TSC chairs for their agreement by email.

The analysis plan will be written once it is felt no further amendments to the protocol are likely. Discussions were held as to whether any formal interim analyses were planned and what might trigger a need for an additional interim analysis. The TSC proposed that a formal interim analysis will not be done unless there is a specific reason to do so. This should be stated in the DMEC charter.

ACTION 19: [redacted] to ensure that the TMG, TSC and DMEC approve the Statistical Analysis Plan prior to commencing analysis to demonstrate that the plan was developed independently of the data.

ACTION 20: Whilst no formal interim analysis is planned, it was agreed that the DMEC should include in their Charter: any possible reasons why an interim analysis might be performed and what would happen in the event of an interim analysis being requested.

The TSC suggested that the TMG consider methods for keeping people interested in the trial, both participants and staff. The issue of summer and Christmas holidays was raised as time periods where the TMG could expect a slower rate of recruitment.

The TSC would also like the TMG to consider issues of staff retention/motivation:

- newsletters
- a monthly update e-mail to all trial staff
- incentives for centres to encourage healthy competition (if centres want this).

It was reported that a PACE day for staff had already been proposed for the end of August – the second wave centre staff will hopefully all be in post by this time.

ACTION 21: [redacted] to continue sending monthly update emails out to all trial staff and to begin producing newsletters for the trial.

The PIs have noticed that the therapists talk across teams and that this has been both a positive and negative thing. When [redacted] it affected the whole team across the country, but following this, the contingency plan put in place by the therapists to cover the absence of a therapist had a positive affect across the whole trial team.

The PIs note that the doctors are the hardest staff group to keep interested in the trial particularly where they rotate periodically. Regular team meetings for the PACE teams (including recruiting and assessing doctors) within centres are being used to keep interest and awareness of the trial high.

The TSC would like to record their congratulations to all staff that the trial is recruiting to target.

6. Contingency policy for absent therapist

a) Absence due to long term sickness, maternity leave or resignation

The PIs presented the proposed contingency policy. The background came in part to deal with a situation which arose when a therapist at [redacted] resigned but had already been considered because of holidays. The PIs explained that an amendment would be sent to MREC regarding this issue incorporating the decisions made by the TSC at this meeting.

The resignation of the [redacted] was especially difficult because of the geographical location of the centre. The PIs reported that the [redacted] GET therapist [redacted] and the [redacted] CBT therapist [redacted] had both generously offered their time to overcome this problem. The [redacted] took over the [redacted] GET caseload whilst the CBT therapist acted as therapy assistant and was learning to give GET. The participants have had all of their therapy delivered by these two therapists in combination. [redacted] has either travelled to [redacted] to give sessions with [redacted] sitting in as a physiotherapy assistant and observer, or [redacted] has given telephone sessions with the participants sitting with [redacted] in the [redacted] hospital for support. As [redacted] is trained up, [redacted] will take a more supervisory role in these sessions and [redacted] will lead them. The PIs reported that the participants affected have responded well to this and are happy with the arrangement.

A new GET therapist for [redacted] has recently been recruited and will be trained over the coming months.

The PIs explained the original rationale in the trial design for dividing the therapies by clinical discipline (i.e. APT delivered by an occupational therapist, CBT by a psychologist or CBT nurse specialist and GET given by a physiotherapist). This was to help ensure clear distinction between the three supplementary therapies. The TMG now feel that disciplines can cross-cover; there are some core clinical skills common to all and the therapists have no difficulty differentiating between each treatment. It was felt sensible in the long term to have cross cover because if one treatment is shown to have a greater efficacy than the others then it will avoid the issue of one clinical discipline 'owning' the best therapy. This will require some minor amendments to the therapy manuals which currently define the discipline delivering each therapy.

ACTION 22: [redacted] to include the changes to therapy manuals in the MREC amendment.

The DMEC had given consideration to the plans at their morning meeting and were happy with distant cover and cross cover, but not happy with the suggestion that a participant could be randomised to receive one therapy but be given another if the therapist was unavailable. They would prefer to suspend recruitment at the affected centre until another therapist was recruited.

The TSC would not recommending suspending recruitment to all the groups in a centre as this could affect staff morale and take the centre a long time to get back up and running to full capacity. The TSC would however consider temporary suspension of randomisation to one therapy within a centre as a preferable solution.

[redacted] spoke to the potential problems if this happened, these include: patients might agree to the trial because a particular therapy was no longer on offer and therefore there might be differences in the population recruited; and unless the minimisation algorithm is changed, not randomising to intervention X in one centre would mean that intervention X would be assigned more frequently to the other centres to preserve the overall balance of assignments between intervention groups which would have practical implications for the trial.

[redacted]

There was some discussion regarding the difficulty of keeping staff in post in some of the disciplines because remaining a long time in a post is contrary to normal career structure and progression.

The PIs asked for TSC approval to train therapists to cross-cover following the successful implementation of this system in [redacted]. The TSC endorsed the plan, believing it to reflect actual practice and supported the concept that no single discipline owns a therapy. A note of caution was made that Physiotherapists and Exercise Physiologists often have a different idea of what is meant by 'graded' and this may need careful monitoring.

ACTION 23: [redacted] to include the cross-cover plans in the amendment to MREC.

The TSC asked whether the anti-PACE campaign has impacted on staff at all. The PIs reported that there was no evidence of this and as yet no trial staff has been directly contacted with the exception of those already known to the campaign groups (i.e. some of the PIs and one of the treatment leaders).

The TSC commented that the TMG should consider the following:

- [redacted] survey of GET & CBT as considered by a small number of surveyed members (not sure what this means). It was found that patients who GET given by OT's reported more negative outcomes than GET given by other disciplines.

- Therapist cross cover will make any analysis incorporating clustering induced by a therapist effect more difficult.

b) Holiday cover arrangements

The PIs explained the contingency that the TMG are proposing for dealing with holiday cover for a therapist. It was recognised that a flexible approach should be taken. In summary, the plan is that where someone is on leave for:

- *Less than 3 weeks* the therapist will attempt to fit in the missed sessions within the five month treatment period but that no more than one session will take place in any one week. This is particularly important for GET where a high frequency of sessions might be too much of a burden to the participant.
- *3 weeks or more* someone else will conduct the missed session.

There has been discussion as to whether the covering therapist should retain a participant taken on where there is more than three weeks holiday, or whether the covering therapist may hand the participant over to the local centre therapist when they return from holiday. Flexibility is advised here with it being recognised that an increasing trial case load may make retaining a participant difficult for a covering therapist, but that it might be more disruptive to the participant to change therapist. Whatever happens should be carefully documented for each case.

The TSC raised a concern about how many sessions should be given by telephone and stated that as per protocol, this should ideally not exceed four sessions. The TSC accepted telephone sessions may be given where the participant sits with a local centre cross-cover therapist whilst receiving a telephone consultation from a distant same-discipline therapist as has been piloted in [redacted].

ACTION 24: [redacted] to send MREC amendment to [redacted] first to ensure it reflects what the TSC have agreed.

7. PACE trial ancillary studies

For future meetings the TSC would like a written summary of all proposed ancillary studies. The TSC recommend that the TMG keep a register detailing:

- Number of participants to be involved
- Any measures that will be taken that are additional to those used in PACE (presented as a chart so that additional participant load can be monitored)
- Whether the study conduct or results could have any impact upon PACE
- Arrangements for ensuring that participants are not being included in several sub-studies if this puts an excessive load on them

ACTION 25: PIs and [redacted] to maintain a register of ancillary studies and to provide a summary report for each TSC meeting.

a) PACE trial ancillary studies approved by the TMG (Genomics study, therapeutic process)

Genomics study

There are four blood samples to be taken across the 52 weeks that the participant is involved in the trial. The TMG did not think taking blood samples would be a problem and had given this study team approval to develop the protocol further. The TSC suggested that the MREC might be concerned about the extra demand on participants with multiple blood samples. The committee also had a number of other questions relating to sample size, power, whether this would require an equal number of participants from each of the four PACE treatment groups and the number of blood samples required.

ACTION 26: [redacted] to collate questions from TSC to take to [redacted] and the genomics study group about the proposed sub-study.

ACTION 27: [redacted] to review the power and sample size for the genomics proposal and advise the TMG. The TMG then to re-consider the proposal.

ACTION 28: [redacted] to seek a peer review of the genomics study from an expert in genetics.

Therapeutic Interaction

The PIs raised a few items for the TSC to consider when reviewing this proposal:

- Would this study require participants to sign a separate consent?
- The discourse analysts would need to know the outcome data of the main trial

The TSC stated that the outcome data can only be released after the main analysis has been submitted for publication. Before this a certain amount of analysis could be completed without knowledge of the outcome data.

In addition, the TSC made the following comments:

- *Ethical issues* - A consent form would be required to be signed by the therapists. It might be difficult to argue that the therapists wouldn't feel coerced into giving their consent, however the fact that the actual analyses are being carried out by people not working on PACE may make it more acceptable
- *TMG approval* - TSC approval would be subject to TMG approval

b) PACE trial ancillary studies awaiting approval by the TMG (Experience of a trial and Two year follow-up studies)

Patient perspective

The PIs explained that the TMG raised a question about sampling which needs to be resolved. The load to the participants will be one extra interview after the 52 week assessment. The interview style is open allowing the participants to speak freely about PACE.

The main concern that the TSC had with this study was over whether there could be an interaction between this and the 2-year follow-up study. This would need to resolved before the TSC could approve it.

ACTION 29: The TMG were advised to reconsider this study in terms of whether it would impact on the two year follow up study [further discussion below].

2-year follow-up

This study was supported in principle. However the complexity of the proposed analysis was noted and it was suggested that the primary analysis should only be based on randomisation. The TSC suggested that a longer period of follow up should also be considered.

The PIs asked whether the TSC would be better placed to decide which sub studies are accepted because the PIs may have personal interest in one or more of the studies and should therefore not judge. The TSC would be willing to take the decision but would require more information on each proposal.

It was noted that the two year follow up study and patient perspective studies could both be carried out only if the 2 year follow-up data were collected and the patient prospective study was completed within the lifetime of the trial unless additional funding was sought. This would mean that participants recruited in the last 24 months of recruitment could not be included into the follow-up study.

The TSC also asked that the study team consider what methods they will use to keep participants under follow up after the end of their participation in the main PACE trial.

Summary

- TSC would like to see a report from the TMG summarising each of the proposals. They are concerned about the cumulative burden on participants.
- For each proposal, the TMG should:
    - Consider whether the sub-studies interact with each other and in what ways
    - Present a timeline showing PACE and the sub-studies
    - Include details of the sample of PACE participants to be used.

8. Any available results (pooled)

The TSC asked whether there was any information available yet regarding the distribution of the participants are at baseline according to the different CFS/ME criteria. [redacted] presented the information as the proportion of participants fulfilling the different criteria:

100% = Oxford

57% = London

76% = CDC

Additionally:

29% = current depressive disorder (a stratification factor)

This is based on only 30 participants and may therefore change considerably over time.

The TSC would like to know what the overlap is between the definitions at future meetings.

9. Organisational issues

Rotation of TMG meetings to include each participating centre

The PIs spoke about a recent TMG meeting which was held in [redacted] and explained the value to be had from holding these meetings at each participating centre rather than basing them in one alone. Also discussed was the fact that TMGs have been opened up to local PACE staff to observe if they wish. Costs of the meetings do increase due to the extra travel involved to facilitate this happening, and whilst money for this has not been included in the original grant, the TMG believe this is valuable for building and maintaining the team. This was pointed out to the MRC staff present.

The TSC endorsed the rotation of TMGs and thought it useful to include local staff. The TSC suggested teleconferences be considered to reduce costs but if these were used to continue to have alternate meetings as face to face

Unused salary funds

The PIs asked whether it is permissible to utilise monies not spent on salaries (i.e. where there is a break between changeover of staff) for other trial purposes. The MRC confirmed that the salary costs may be vired but care should be taken in viring between staff and non staff costs as it has implications for overheads. If in doubt they should be consulted,

Second wave centres

Some issues with the institutions involved in PACE at Oxford which might delay start of this centre were discussed.

The TSC suggested that the second wave centre leaders are invited to sit in as observers to the TSC meetings. It was clarified that they may not be voting members because the formal TSC membership must have a majority (> 50%)

of independent members. It is especially important to adhere to this because of the publicity surrounding the trial. It was also noted that [redacted] of the [redacted] sits on both the PACE and FINE TSCs. (Cross representation of the FINE and PACE PIs on each other's committees was also considered desirable if possible).

10. Public relations

MRC receive a lot of correspondence amounting to several letters a week regarding the PACE and FINE trials. Some of these are direct correspondence and others come as queries sent via local MP's. The MRC Head Office offer support to all staff involved in the trial and reinforces the recommendation that if anyone should receive any correspondence they should pass this on to the MRC press office to answer.

ACTION 30: The MRC request that when time allows a PACE trial website be launched that will answer some of the common questions.

ACTION 31: The MRC recommend that an abridged version of the protocol be published soon.

ACTION 32: [redacted] to speak to MRC for advice on how much of the protocol should be published.

11. ISRCTN registration

The issue was discussed as to whether or not registration with the ISRCTN is considered sufficient to enable the TMG to publish the PACE results in an International Committee of Medical Journal Editors (ICMJE) journal. The MRC stated that at present all MRC trials are registered with ISCRCTN only. It was recommended that the TMG keep an eye on this situation and consider registering with The Lancet as well.

ACTION 33: TMG to consider registering PACE with the Lancet.

12. Any other business

<u>Definition of a new patient</u>

The PIs raised the issues that, according to the protocol, patients are ineligible for PACE if they have received one of the trial treatments before for CFS/ME. The PIs on behalf of the TMG raised the issue of whether to define what constitutes having received Standardised Specialist Medical Care (SSMC) before. They propose that a new patient be defined as someone who has not received more than three sessions in a secondary fatigue clinic with a fatigue clinic specialist.

The TSC suggests the PIs consider this on a case-by-case basis as this was difficult to define. The TSC recommend the PIs establish whether each new patient has received a treatment close to SSMC in the past and to establish a

time frame within which change, as a result of a treatment, would have been expected.

ACTION 34: PIs to consider this matter further and provide an operationalised definition.

13. Date of next meeting

The TSC would like to meet again after six months and once the second wave centres have opened to recruitment. Two dates have been suggested of the 23rd or 24th January.

ACTION 35: [redacted] to offer both dates to TSC members who were unable to attend this meeting and confirm the availability of all other members.

[redacted] 13.07.2005

Summary of ACTION Points

DMEC

ACTION 20: Whilst no formal interim analysis is planned, it was a greed that the DMEC should include in their Charter: any possible reasons why an interim analysis might be performed and what would happen in the event of an interim analysis being requested.

PIs/TMG

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ACTION 2: PI's with help of the statisticians and DMEC, to consider how best to measure life participation.

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ACTION 18: [redacted] and the PIs to develop the format for this report to show to DMEC and TSC chairs for their agreement by email.

ACTION 19: [redacted] to ensure that the TMG, TSC and DMEC approve the Statistical Analysis Plan prior to commencing analysis to demonstrate that the plan was developed independently of the data.

[redacted]

ACTION 1: The PIs in conjunction with [redacted] to respond to the DMEC request to develop an operational definition of serious deterioration. This definition should be sent to the DMEC & TSC for comment by email rather than wait for next meeting.

ACTION 2: PI's with help of the statisticians and DMEC, to consider how best to measure life participation.

ACTION 27: [redacted] to review the power and sample size for the genomics proposal and advise the TMG. The TMG then to re-consider the proposal.