# Supporting document by Mr Matthees to the Information Commissioner's Office for the Freedom of Information request titled 'Timing of changes to PACE Trial recovery criteria' (2014).

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This supporting document has been broken up into sections to make it easier to follow:

**• Previous correspondence with QMUL in relation to this FOI request**

**• The FOIA should cover the requested information sought**

**• This FOI request does not quality to be judged as 'vexatious'**

**• Further background information (if necessary)**

**• Comments on the issue of QMUL receiving FOI requests**

**• Concluding statement for this appeal to the ICO**

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## Previous correspondence with QMUL in relation to this FOI request

On the 26th April 2014 I submitted a FOI request through the WhatDoTheyKnow.com website, a commonly used and legitimate medium for publicly utilising the FOIA. This website was used to get clear answers on the public record. QMUL acknowledged this request within a few days and later responded in full on the 28th May 2014 (24 working days after the request). QMUL had refused the FOI request under Section 14(1) i.e. on grounds that it was (allegedly) "vexatious", which I think was unreasonable.

On the 18th July 2014 (another 38 working days later), I asked for an internal review of the handling of this FOI request and provided a detailed explanation for why I believe it was valid, important, and not vexatious. By the 12th September 2014 (another 40 working days later) I had not received a response, so I sent a reminder and further supporting explanations.

On the 24th September 2014 (48 working days after the request for an internal review) QMUL wrote that the refusal was upheld by the internal reviewer and apologised for the delay. I found this to be unreasonable, so I decided to contact the ICO.

All this previous correspondence with QMUL can be found here:
https://www.whatdotheyknow.com/request/timing_of_changes_to_pace_trial

I used the following website to determine the passing of working days:
http://www.work-day.co.uk

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## The FOIA should cover the requested information sought

The Freedom of Information Act 2000 (FOIA) provides public access to information held by public authorities. Members of the public are entitled to request information from these public authorities (who are obliged to respond appropriately). Unless there is an overriding exemption, which I highly doubt in this case, the FOIA covers all recorded information held by a public authority. All the information relevant to this FOI request should be recorded in some form or another at QMUL:

^ http://ico.org.uk/for_organisations/freedom_of_information/guide/act

According to a 'Freedom of Information and Research Data Q&A':

*"The Freedom of Information Acts and Environmental Information Regulations are designed to ensure accountability and good governance in public authorities. Most UK universities are defined as public authorities, and thus have a legal obligation to disclose information unless the law specifically provides a reason why they need not. In other words, unless there is an overriding reason for not providing information to the public, you must provide it. The reasons the law will consider as acceptable are contained in the FoI Acts as 'exemptions' and the EIRs as 'exceptions'."*

^ http://www.jisc.ac.uk/media/documents/publications/programme/2010/foiresearchdata.pdf

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## This FOI request does not qualify to be judged as 'vexatious'

I have generally followed the ICO guidelines on 'How to access information from a public body':

^ http://ico.org.uk/for_the_public/official_information

As a public authority, QMUL are legally obliged to respond appropriately to each request made under the FOIA. I do not believe that QMUL has responded appropriately to my FOI request. It was an attempt to clarify ambiguities, but QMUL dismissed it as "vexatious", which I believe was unreasonable. To help understand why it was refused on these grounds, I have examined two ICO specialist guides and found no significant reason why this FOI request can be genuinely judged to be "vexatious":

http://ico.org.uk/~/media/documents/library/Freedom_of_Information/Detailed_specialist_guides/vexatious_and_repeated_requests.pdf

http://ico.org.uk/~/media/documents/library/Freedom_of_Information/Detailed_specialist_guides/dealing-with-vexatious-requests.pdf

I have outlined the key points made in these documents in my previous correspondence with QMUL. The given indicators of vexatiousness are not meant to be a list of qualifying criteria, but only a guideline for the public authority's judgement. Nevertheless, the list and description of indicators do not match the characteristics of this FOI request, which has certainly not been a "manifestly unjustified, inappropriate or improper use of a formal procedure". Much of the above mentioned guidance is focused on whether there is a "disproportionate or unjustified level of disruption, irritation or distress", in relation to the request itself and its inherent purpose. According to the ICO specialist guide, 'Dealing with vexatious requests (section 14)', the ICO will be primarily looking for evidence that the FOI request would have an unjustified or disproportionate effect on the authority:

Therefore, *"the authority should therefore be able to outline the detrimental impact of compliance and also explain why this would be unjustified or disproportionate in relation to the request itself and its inherent purpose or value. Where the authority believes that the context or history strengthens their argument that the request is vexatious, then we would also expect them to provide any relevant documentary evidence or background information to support this claim."*

^ http://ico.org.uk/~/media/documents/library/Freedom_of_Information/Detailed_specialist_guides/dealing-with-vexatious-requests.pdf

In my opinion it is highly unlikely that fulfilling this FOI request would have an unjustified or disproportionate effect on QMUL in terms of the level of disruption, irritation or distress caused, in relation to the purpose of this FOI request. I also highly doubt that asking a few questions would be exempted by s.12 (exceed cost limits i.e. £450, calculated as the estimated cost of one person spending 18 hours in determining whether the information is held, then locating, retrieving and extracting the information). If it does, I may be prepared to cover the additional costs as long as they are based on a reasonable and realistic assessment.

I do not understand how this FOI request could be mistaken by QMUL as genuinely vexatious. With respect to my own efforts, I introduced the FOI request with 4 or 5 relatively brief paragraphs in order to adequately

explain the background situation that justifies the questions asked and the value of the answers sought. The cut off point for evidence of vexatiousness is up to 20 working days after the FOI request was submitted. In a later message after the initial refusal, when countering the indicators of vexatiousness and comparing them to my FOI request, I wrote "Fulfilling this FOI request should only take an email to and from whomever knows this information." This was not meant to instruct QMUL on what to do, but highlight how easily the information could be provided, as it is only asking for routine facts about a clinical trial. If a sentence bordered on displaying accusatory tone, I can provide further references to back it up. I am new to submitting FOI requests to public authorities in the UK, so if there is anything I wrote which was not strictly proper etiquette, or if I have committed any technicality that is immaterial to the overall validity and purpose of this FOI request, I can re-submit a modified version if recommended by the ICO.

The 'wider context' is that this issue involves contentious research, but this alone does not justify invoking s.14. The fact that the PACE Trial has courted some controversy should not distract away from the fundamental purpose of this FOI request, which is to unambiguously resolve the confusion surrounding the timing and nature of protocol changes. There have been numerous articles and other efforts to generally frame the extensive public and academic criticisms of the PACE Trial as a campaign stemming from ideological convictions about ME/CFS and prejudices against mental illness, etc. I will not go into further details about that unless necessary, but during my background research I discovered that QMUL has previously claimed to the ICO that *"the CFS/ME patient community is very close, active and motivated in numerous cases to challenge the outcomes of studies with results which do not comport with their beliefs as to the causes and treatment of CFS/ME"*.

^ http://ico.org.uk/~/media/documents/decisionnotices/2014/fs_50514995.pdf

However, even if any of these allegations were generally true, it is unclear what they have to do with this FOI request, and they certainly do not negate the importance of ensuring that the claims made by public bodies in published academic papers are accurate, transparent, and informative. In the present case, clear answers are sought to resolve ongoing confusion which QMUL shares responsibility in generating. This debate goes beyond the simplistic, speculative, blanket, and stereotypical portrayal of critics belonging to a group who challenge whatever research does not agree with their beliefs. An honest and fair discussion or presentation of the relevant issues at hand is more important than speculations about the beliefs and motivations of others.

My only history with QMUL prior to submitting this FOI request is submitting a previous FOI request about a month earlier. Before submitting this second request I waited 23 working days so that QMUL had adequate time to respond to the first request (which after 20 working days was refused on other exemptions unrelated to s.14) That is not a valid reason to regard this request as vexatious, and as it is a sincere attempt to get clear answers for the questions asked and not an exercise in harassment, QMUL would also have no evidence to support any allegation suggesting that I intended to harass them. If any general or specific allegation or suggestion is made about harassment or intentions, I would appreciate the opportunity to respond. Furthermore, the focus is on the request itself but not the requester, and according to a Freedom of Information and Research Data Q&A:

*"In principle, the FoI Acts and EIR are 'applicant blind and motive blind'. The location, nature and/or motives of the requester are irrelevant. The requester could be anyone: a competitor, a member of the public, someone hostile to your research, a research funder, a member of your Ethics Committee, or anyone else anywhere in the world."*

^ http://www.jisc.ac.uk/publications/programmerelated/2010/foiresearchdata.aspx

QMUL have shown no willingness to engage with me or work out a compromise on the questions asked (which the ICO suggests as an alternative to invoking s.14). Unsurprisingly, I am unsatisfied and disappointed with their overall response.

This FOI request has significant value to me and the ME/CFS community, and according to the ICO, public authorities cannot refuse a request simply because it does not seem to be of much value to them. *"The key question to ask yourself is whether the request is likely to cause a disproportionate or unjustifiable level of*

*distress, disruption or irritation. [...] You should be prepared to find a request vexatious in legitimate circumstances, but you should exercise care when refusing someone's rights in this way."*

^ http://ico.org.uk/for_organisations/freedom_of_information/guide/refusing_a_request

There are no "legitimate circumstances" for invoking s.14 here, and in my opinion QMUL have not exercised care, hence why I have complained to the ICO in the hope of having QMUL's decision reversed. I would not have pursued this FOI request unless I believed that it has significant value, or if adequate reliable information already existed in the public domain.

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## Further background information (if necessary)

According to an article on the ICO website directed at public authorities: *"We cannot investigate other matters that may lie behind the request. We focus on only whether you have complied with the Act."*

^ http://ico.org.uk/for_organisations/freedom_of_information/guide/complaints#what-happens-when-someone-complains-2

I have already provided an explanation and justification for this request in the previous correspondence with QMUL. I do not wish to burden the ICO with technical details about the PACE Trial protocol changes unless it is relevant to deciding the outcome of this complaint. I will provide some additional details below in order to help establish background context to this FOI request. If further information not covered so far is required, then I am happy to provide it by email. I will include some URLs as references or further reading on specific issues but I do not expect the ICO to examine them at length unless necessary:

**The importance of trial protocols**

Numerous articles have been authored on the importance of trial protocols, but I do not need go to into much detail. An editorial by Fiona Godlee was published in BioMed Central (BMC) in 2001, outlining the importance of trial protocols.

^ http://www.biomedcentral.com/content/pdf/1471-8219-2-4.pdf

Recently there has been a lot of publicity around the issue of transparency in clinical trials e.g. the AllTrials campaign, etc. Accordingly, researchers are generally expected to pre-publish their protocols and then report the protocol-defined outcomes, to avoid cherry picking of results and stealth post-hoc revisions. We are told that such methodology and scrutiny is fundamental to the process of good medical science. When protocol changes are made, these should be adequately justified and clearly described.

**The published PACE Trial protocol(s)**

The PACE Trial was a large study into various interventions for Chronic Fatigue Syndrome (CFS). A study protocol was published in BioMed Central during 2007, outlining how the trial was being conducted, and *"BioMed Central believes that publishing study protocols will help to improve the standard of medical research by: [...] Enabling readers to compare what was originally intended with what was actually done, thus preventing both 'data dredging' and post-hoc revisions of study aims."*

^ http://www.biomedcentral.com/authors/protocols

This protocol was published on the basis that it had ethical and funding approval, and that *"the authors/investigators are unlikely to be able to make revisions to their protocol"*. The editor(s) also *"strongly advise readers to contact the authors or compare with any published results article(s) to ensure that no deviations from the protocol occurred during the study."*

^ http://www.biomedcentral.com/imedia/2095594212130588_comment.pdf

The 2007 PACE Trial protocol states: *"A full Analysis Strategy will be developed, independently of looking at the trial database, and before undertaking any analysis. This paper summarises the analysis plan."*

^ http://www.biomedcentral.com/1471-2377/7/6

The Statistical Analysis Plan is a relatively large document further describing the trial protocol and provides some insight into what was changed before the unblinding of trial data, particularly what was later changed or missing from the plan at that stage.

It states that no analyses of outcomes mentioned in the plan were to be conducted prior to final written approval of the analysis strategy by the Trial Steering Committee. The plan also indicated that exploratory papers will not be bounded by the plan, that there may be post-hoc changes or additions to the trial protocol, and that the trial protocol may be updated with guidance from a blind review of trial data i.e. view trial data without being aware which group the summary statistics represent. The various analyses in the plan reveal that the authors will have a very good idea of the distribution of scores for the various outcomes.

^ http://www.trialsjournal.com/content/14/1/386

**The extensive major changes to the 'recovery' criteria**

The primary outcomes at the group level (average fatigue and physical function scores) were changed before the author unblinding and main analyses were conducted, and this change was described in the statistical analysis plan. However, all the thresholds for clinical improvement and recovery on an individual patient level for fatigue and physical function were abandoned and apparently replaced with post-hoc changes or additions after the authors were unblinded to trial data.

Given the above background, many individuals have become concerned that the reported results of the PACE Trial have involved major changes to the protocol which may not be justified or approved, introduced post-hoc after being unblinded to data, and that many pre-defined outcomes still remain unpublished several years after completion of the main data collection period.

Without listing or referencing all the criticisms made against the trial, the revised definition for 'recovery' from CFS underwent extensive major changes (not just one or two changes but most if not all criteria were significantly weakened or relaxed). This would have a major effect on the estimated rates of participants classified as completely 'recovered' at 52 week followup. None of these changes or additions to the protocol were in the final version of the statistical analysis plan.

According to Leonard Jason (researcher and professor of psychology at DePaul University in Chicago), *"Other researchers have been critical of that trial, however. A number of experts have taken issue with the authors' definition of recovery, Jason says."*

^ http://www.apamonitor-digital.org/apamonitor/201410#pg72

The 2007 PACE Trial protocol states: *"Recovery" will be defined by meeting all four of the following criteria: (i) a Chalder Fatigue Questionnaire score of 3 or less, (ii) SF-36 physical Function score of 85 or above, (iii) a CGI score of 1, and (iv) the participant no longer meets Oxford criteria for CFS, CDC criteria for CFS [1] or the London criteria for ME.*

^ http://www.biomedcentral.com/1471-2377/7/6

In the published paper on 'recovery' from CFS: criterion (i) was significantly loosened to a CFQ (bimodal scoring changed to Likert) of ≤ 18 points; criterion (ii) was greatly lowered to a SF-36 physical function score of ≥ 60 points; criterion (iii) was significantly loosened to allow a CGI score of either 1 or 2; criterion (iv) was significantly loosened by disqualifying a participant from meeting Oxford criteria if they failed any of the fatigue or physical function entry criteria regardless whether they otherwise still met Oxford criteria (this ad

hoc modification is not a part of the Oxford criteria), the CDC criteria was not applied properly, and one of the key authors to the London criteria for ME has publicly denounced (on PubMed Commons) the version used in the trial.

^ http://www.ncbi.nlm.nih.gov/pubmed/23363640
^ http://www.ncbi.nlm.nih.gov/pubmed/21334061#cm21334061_1177

These extensive major changes are the primary reason why the revised definition for 'recovery' from CFS has been questioned, on the basis that the thresholds used for the 'normal range' in fatigue and physical function had overlapped with mandatory trial eligibility criteria for severe chronic disabling fatigue, that the criteria of no longer meeting CFS criteria does not guarantee not having CFS, that a modest improvement is not the same as a full recovery, that it was possible for a participant to be classified as 'recovered' without a clinically significant improvement in the primary outcome measures of fatigue and physical function, and that these optimistic recovery rates are inconsistent with the objective evidence available.

An in-depth analysis of the protocol changes goes beyond the scope of this FOI request, as it is focused on information about the timing and nature of changes to the protocol, requested in order to help clear up the confusion on these issues. Again, I am happy to discuss these issues at greater depth by email if needed. Of particular note was how the threshold for normal physical function was decreased so much that it became lower than the trial eligibility criteria for significant disability. The stated justification for this change is demonstrably erroneous and therefore highlights that merely stating a reason for change is no guarantee it is justified, and also questions the notion that the change was made after thoughtful consideration.

Several letters to the editor were published in response to the paper on recovery from CFS in the PACE Trial:

^ http://www.meassociation.org.uk/2013/07/pace-trial-letters-and-reply-journal-of-psychological-medicine-august-2013

A series of BMJ Rapid Responses (moderated e-letters) have been published discussing these changes:

^ http://www.bmj.com/content/347/bmj.f5963/rapid-responses

The timing of these changes strongly suggest that they occurred after the authors had been unblinded to a range of trial data. This would mean that changes have been made without adequately labelling them as post-hoc in the published paper. Similarly, confusion has also arisen over which changes were approved by the relevant oversight bodies. This confusion about the timing and nature of the changes has risen to the level of parliamentary debate, and I do not believe the issue was settled there, because some of the information appears to be second or third hand, inaccurate, and/or conflicts with the more official sources available.

While the problems outlined above are important context, the core issue of this FOI request is about the confusion that has arisen over the timing and nature of changes to the protocol. My questions relate to how this change came about and when it was approved, as this is unclear in the published papers. I believe it is in the public interest that information from a clinical trial is published according to the pre-defined protocol, and where changes are made the reasons and authority for the changes are clear, sensible and verifiable. It is not vexatious to ask for answers on this issue to clarify the ongoing confusion.

Contrary to a statement made by QMUL on the protocol changes, none of the changes made the recovery criteria "more stringent", and the above circumstances cast doubt on whether "these changes were made before analysing any data".

^ https://www.whatdotheyknow.com/request/pace_trial_recovery_rates_and_po#incoming-327302

I want to clear up this ongoing confusion with unambiguous answers from QMUL.

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## Comments on the issue of QMUL receiving FOI requests

In a recent paper, Professor White (principal investigator of the PACE Trial) co-wrote: *"A large number of Freedom of Information Act requests seeking information on all aspects of the trial."*

^ http://pb.rcpsych.org/content/early/2014/07/14/pb.bp.113.045005.full.pdf+html

I do not know why QMUL dismissed my FOI request as vexatious or what evidence they could possibly have to persuade the ICO to support the original judgement of vexatiousness. After doing some research I began to suspect that QMUL may raise the issue of the number of FOI requests they have received in relation to the trial in general. Although this issue has nothing to do with me specifically as my FOI request was made independently from other requests or requesters, I wish to comment on the issue anyway because QMUL may raise the issue in their defence and therefore it may become important when the ICO evaluates the wider context of the general circumstances in which this FOI request was generated.

I have previously described the scenario in which numerous individuals have become concerned about changes to the trial protocol. Major deviations from the published trial protocol and genuine concerns over the contribution of these changes may have naturally led to a number of FOI requests to QMUL, particularly when combined with the following factors:

There are an estimated 250,000 patients with ME/CFS in the UK, and an estimated 17 million globally. The PACE Trial was perhaps the largest study on CFS in the UK's history (in terms of allocated resources and publicity), and it has been repeatedly presented to audiences as giving 'definitive' answers on the management of CFS. Details about FOI requests are not usually made public, so it is likely that many independent requests have shared common themes because multiple individuals arrived at similar conclusions or had similar questions based on the limited public information available. BioMed Central had encouraged its readers to contact the authors to make sure the protocol had been followed properly in the trial. Some people may not be aware that merely asking for any information via email to QMUL or the PACE authors may be treated as a formal request under the FOIA.

Therefore, the number of FOI requests submitted to QMUL overall may relate largely to the quality of the published measures, the remaining questions or ambiguities that have arisen, the technical concerns about the changes to the trial protocol, and the failure to release information on established outcomes as promised in the trial protocol. QMUL should consider the extent of which oversights on its behalf have contributed to these FOI requests being generated.

The several FOI requests made publicly by individuals through the WhatDoTheyKnow.com website have generally sought the trial results as outlined in the trial protocol, or which would provide important context to information already published i.e. summary statistics on the 'recovered' participants as a group. These efforts appear to reflect an understandable expectation to see the PACE Trial stand up to its own pre-defined protocol or to better establish the efficacy of the interventions tested.

^ https://www.whatdotheyknow.com/search/%22PACE%20Trial%22%20CFS/all

When using the WhatDoTheyKnow website I recently noticed that a separate FOI request made independently by someone else (Anna Sheridan) was also dismissed by QMUL as "vexatious" under Section 14(1), even though her request was recommended by the Information Commissioner. After she asked for an internal review and pointed out that her request was recommended, QMUL changed the exemption to s.12 (cost limitations). This raises the question of why it was mistakenly judged as "vexatious":

^ https://www.whatdotheyknow.com/request/raw_data_for_6mwt

As a public authority, QMUL are obliged to respond appropriately to each request made under the FOIA. I do not believe that QMUL has responded appropriately to my independent request by dismissing it as "vexatious" (and taking 24 working days to do so). I hope that QMUL do not treat FOI requests with contempt or have lowered their standards of consideration given to each one.

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## Concluding statement for this appeal to the ICO

The FOIA covers the requested information because it should be recorded at QMUL, a public authority which accepted £5M of public funding for a large trial and the responsibility which goes with it. This FOI request was not vexatious and is a valid attempt to resolve specific ambiguities relating to the timing and nature of major protocol changes to the PACE Trial. The genuine purpose of this FOI request has been justified in previous correspondence with QMUL and in the further explanations provided above. It is important that unambiguous answers from QMUL go on the public record about the issues highlighted by this FOI request.

Requests made under the FOIA are not something which should only be granted in rare cases; public authorities are legally obliged to disclose any requested information for every single case unless there is a good overriding reason not to. I have only asked a few relatively simple but important questions to help resolve ongoing confusion about a high-profile trial. Fulfilling this FOI request should be relatively easy, the public has a right to this information, and there is no legitimate reason for QMUL to refuse disclosure.

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