To: Office of Disease Prevention
National Institutes of Health
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re.: December 9–10, 2014 **DRAFT EXECUTIVE SUMMARY** P2P workshop by Carmen R. Green, M.D.; Penny Cowan; Ronit Elk, Ph.D.; Kathleen M. O'Neil, M.D.; Angela L. Rasmussen, Ph.D.

Den Bosch, The Netherlands, January 12, 2015

Dear mrs. Watson,

First of all we would like to thank you for at least trying to take a step forward in better serving the indeed underserved ME/CFS community which as the P2P-panel concluded has lead to a stigmatization of patients including social isolation and judgment with all consequences involved, as is rightly stated in the summary of the concept report of the P2P-workshop of December 9-10, 2014 (http://bit.ly/1A6Q8IK, 120-124), for over 35 years already.

We have carefully read the summary and would like to start our comment with three straight and clear advices.

1. The NIH should take stock of the present research and researchers in the field, and coordinate their cooperation by strongly funding their replica and extension studies.

2. The NIH should consent with the international research agreements to use either the CCC or the ICC for research and clinical purposes, for the time being, until new facts are found which justify an alteration of either of them.

3. Patients should not be pressed but only be invited to cooperate with a body which seems to have left them alone for decades, causing many an untimely death and untold suffering (326-327, 357). Instead an attitude of service, compassion and apology should be adopted by both the NIH and the HHS as well as all researchers involved. Patients and patient advocates and organizations should be invited to take part in decision making and developing treatments and strategies and have a strong say in the matter, as there's a treasure-house of experience there. However no pressure should be enforced on any patient anymore, as it is a core feature of the disease that this is known to increase disease severity.

The report suggests that there is a relatively small number of researchers in the field and finite resources (328-329). The last part is definitely true and is the actual reason no cause of the disease nor markers for it and consequently no drugs to combat it have been discovered as yet. Presently there are ample researchers and research centers and it would be a great step forwards if the NIH would pledge to take stock of which research on which aspect of this multi-system disease has been done and is being done by now by whom, thus creating a possibility to fund steps that are already being taken most efficiently, instead of starting the whole research-progress all over which would mean a setback of decennia. The actual problem is that very much *has* been discovered already about the disease in

pilot studies, but no research money has been available to do reproduction and extension studies, like in Norway the 3rd phase rituximab-study is being done due to funding of the Norwegian government. It would save time and money if the NIH would decide to build on existing outcomes and research already been done by existing disease-experts. Several members of the P2P-panel are very well informed which scientists and clinicians would be in a position to execute reproduction studies as well as phase 2 & 3 studies.

Moreover the summary is suggesting there is no consensus about the research criteria to be used (34-37) and rightly concludes the Oxford-criteria are impairing progress and causing harm (378-379). But there is consensus amongst all scientists and clinicians doing research at this very moment about common research-criteria being used and to be used until new discoveries have been made. In a letter of December 26, 2013 of 197 scientists, patients and patient advocates to the then secretary of health hon.mrs. Sebelius re. the contract of the HHS with the IOM to redefine the disease, they clearly stated there's agreement on using the Canadian Consensus Criteria of 2003 and strongly advised her to introduce the ICC of 2011 as these are based on advanced researches and outcomes since 2003.

So it would be but natural to introduce the CCC right now as the basic consensus for further research and clinical practice as many symptoms have been discovered already and are being dealt with, at the financial costs of the patients themselves, as they are not recognized as such. The only strategy mentioned in the draft stated to have modest benefit, i.e. CBT (362), is contradictory to the context of the draft which states no measures are available to diagnose or treat ME/CFS. Many severely ill patients are known to have suffered increased disease symptoms due to enforced CBT and GET, risking their income and health insurance provisions when refusing the therapy. A new consensus on the disease may be considered when research offers new outcomes.

Thirdly, on several places in the draft there's pressure on patients to participate actively in care and decision making (326-327, 357). It is characteristic of the disease that patients need the little energy left –if any – to survive and find out their own strategies and treatments, at high costs in money and energy. It is improper to ask their cooperation at the onset whilst not having done substantial efforts yet to take the steps drawn in this draft. That would be asking for blind faith. They cannot be expected to have trust in the NIH and its suggestions while being left alone for decades, totally dependent on the discretion of their GP, therapists and specialists, often labeled as psychosomatic cases , maintaining their symptoms through their own perception, which is outrageous. Young women and men are known to have been separated from their homes forcibly and outplaced in foster care or even psychiatric wards just because they weren't able to attend school because of total lack of energy due to ME/CFS.

Now we will comment on the draft itself in order of sequence:

3: Post Exertional Malaise (PEM), not fatigue is the core symptom of the disease.

5-6: how can the economic burden and prevalence of ME be estimated when there's no consensus about the disease criteria?

33-34: there are clear distinguishing markers between ME/CFS and Major Depressive Disorder.

58: *Fatigue has* **wrongly** *been the defining focus of recent research*. This has caused decennia of delay of focus on right parameters to be researched effectively.

63: *Limited research dollars directed at ME/CFS* is the essential problem. Otherwise the riddle had since long been solved.

89. *Clinical studies have … focused on … Caucasian … women*. Which research is being spoken of here? As far as we know, the cohorts have been versatile with every research, a vague mixture of the Fukuda criteria and the CCC being the only access criteria.

95. *Focusing on fatigue alone may identify many ME/CFS cases*. This is totally wrong and exactly the core problem why this panel has been created. Focusing n fatigue may include all patients of other diseases in which fatigue predominates.

113-114: CBT and GET demonstrate only improvement in persons who do not meet the CCC or ICC. In mildly to severely ill patients it is proven to work counterproductive. It indeed is hazardous to enforce treatments on patients who are not properly diagnosed, including the actual causes of impaired cognitive functioning.

147: That's exactly what the CCC and ICC are doing already: carefully defining comorbid conditions.

166: The symptoms patients consider clinically meaningful ARE in the scientific literature, in pilot studies, but due to lack of funding by the HHS and the NIH couldn't be confirmed by replica studies. The community isn't really a good source for crowdfunding, as patients spend all their money on therapies which may help but are not covered by insurance companies.

204-211: Who is going to develop a national and international research network etc? Based on which data and criteria scientists will be included?

235-236: Biobanks are already in existence and developing fast with experienced knowledge of which biologic samples should be collected, based on CCC-research. Previously collected research data should be analyzed indeed, as stated in 248-249. This is crucial.

270: Underscoring *longitudinal studies* means many more years of waiting for the community for markers and drugs. Longitudinal studies may be necessary for evidence based conclusions but much has been discovered about the disease which is already helping patients, among which drugs which presently have already been approved by the FDA and are being used in other conditions. Application of such drugs should go hand in hand with longitudinal studies, lest many more patients will not die before a diagnostic tool may be discovered and developed.

293: …*measures developed by the NIH*… Does this exclude measures developed outside the NIH? If PROMIS is being used here, it should at least go along with research and clinically confirmed criteria.

296-302: Again as in 293 this is excluding existing scientific achievements by focusing completely on the resources of the NIH.

306: Online tracking tools are not accessible to mild to severe patients because of cognitive impairment and quick overload of sensitive impulses. Severe patients do not stand a pc and have no access to the internet.

312-313: *primary care clinicians……referred to appropriate specialists*… who in turn have little to no knowledge of ME/CFS…

330 *New collaborative models*: as suggested earlier, first of all take stock of existing ones, thus saving precious energy, precious time and precious funds.

350-351: First of all use already existing archives.

365-366: Who will decide on who's going to be invited on the meetings mentioned here? Do patients finally have a say in this, as they know best which researchers are doing significant and even groundbreaking research on their disease? Did patients have a say in the make-up of this P2P-panel?

380: As reiterated several times already, the ME/CFS community *does* already agree on a single case definition, being either the CCC or the ICC developed from the CCC. Start using them as long as no new markers are discovered.

385: *multimodal therapy* should be very carefully defined, not overemphasizing the role of psychiatry which has done so much harm to the community already. ME/CFS being a multi-system disease treatment of one set of symptoms should be carefully monitored as it may cause an increase of other (groups of) symptoms.

To conclude with our suggestions once more:

1. 1. The NIH should take stock of the present research and researchers in the field, and coordinate their cooperation by strongly funding their replica and extension studies.

2. The NIH should consent with the international research agreements to use either the CCC or the ICC for research and clinical purposes, for the time being, until new facts are found which justify an alteration of either of them.

3. Patients should not be pressed but only be invited to cooperate with a body which seems to have left them alone for decades, causing many an untimely death and untold suffering (326-327, 357). Instead an attitude of service, compassion and apology should be adopted by both the NIH and the HHS as well as all researchers involved. Patients and patient advocates and organizations should be invited to take part in decision making and developing treatments and strategies and have a strong say in the matter, as there's a treasure-house of experience there. However no pressure should be enforced on any patient anymore, as it is a core feature of the disease that this is known to increase disease severity.

We do hope you will take this comments most seriously, and again would like to thank you for the opportunity. That is one step in the right direction. Doing something with it would be a second, vitally more important step.

With kind regards,

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