TO: Office of Disease Prevention, National Institutes of Health

FROM: James H. Mills

DATE SUBMITTED: January 14, 2015

RE: Public Comments on 2014 NIH Pathways to Prevention Workshop: Advancing the Research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

The following comments are based on the Draft Executive Summary containing 389 lines.

1. The following statements from the Report clearly indicate the failure of U.S. public health policy in addressing ME/CFS over thirty (30) years. Our Federal government has abdicated its responsibility to provide leadership in finding a cure for ME. The Panel has the opportunity to change this. It is important to do so.

Line 6, "unmet public health need"; Line 11, "failing to assess and treat the disease"; Line 63, "limited research dollars"; Lines 76-77, "Over the last 20 years, minimal progress has been made to improve the state of science for patients with ME/CFS…"; Line 87, "limited patient and professional education has impaired progress in managing ME/CFS"; Lines 142-143, "Many patients with ME/CFS are misdiagnosed and treated erroneously with potentially toxic therapies that may cause harm and diminish hope."; Lines 168-169, "Current research has neglected many of the biological factors underlying ME/CFS onset and progression."; Lines 181-182, "Overall, there has been a failure to implement what we already know for patients with ME/CFS while it steals their health and well-being."; Line 186, "Innovative biomedical research is urgently needed…"; Lines 197-198, "the potential cause of ME/CFS and possible treatments are poorly understood, and that there are many unresolved issues…"; Lines 214-218, " The NIH Institutes and Centers and other U.S. Department of Health and Human Services (HHS) agencies should coordinate research efforts to promote efficiency and effectiveness…"; Lines 242-243, "there is much to learn by developing a registry/repository of all patients with ME/CFS."; Lines 271-273, "Patients often choose clinical trials or complementary and alternative medicine because effective treatment is not available and because traditional health care is not meeting their needs."; Lines 277-278, "There is critical need for improved measures to identify ME/CFS…"; Lines 281-282, "The NIH should develop an ME/CFS methodological workgroup."; Lines 291-293, "The NIH should leverage the power of other longitudinal studies…to better understand ME/CFS."; Lines 339-343, "The NIH should work with ME/CFS partners and stakeholders to create a website for patient and clinician educational materials as well as information regarding clinical trials. Opportunities to utilize the NIH Clinical Center for clinical trials and to fast-track new therapies should also be explored." Lines 351-352, "We recommend that the NIH and the FDA convene a meeting on the state of ME/CFS treatment."

I believe the Report should begin with a forceful statement acknowledging this failure in addressing ME/CFS over thirty (30) years and stating the need for a concerted effort by NIH to marshal whatever resources are necessary to solve ME/CFS and find a cure.

The Report needs to express how imperative it is to find a cure for ME.

The Panel has an opportunity in its Report to express a vision of what needs to be accomplished to treat and cure ME/CFS. One of the participants at the April, 2011 NIH Workshop on ME/CFS said that something similar to the "Manhattan Project" is needed to find a cure for ME/CFS. I believe the "Manhattan Project" is an apt analogy to consider in describing the bold actions that NIH needs to undertake in order to solve the ME/CFS crisis.

The Report should clearly state that NIH needs to adopt an aggressive, coordinated, fully funded plan to address the ME crisis.

For progress to occur, NIH needs to ensure that patients' voices are heard, adequate research funding is provided, appropriate biomedical research is undertaken, and medical students and practicing physicians are educated about ME.

I believe it is important for the Report to make a statement to this effect.

2. Line 3, "…characterized by extreme fatigue and other symptoms…" and Lines 58-59, "Fatigue has been the defining focus of recent research, but many other symptoms need to be explored, primarily neurocognitive deficit ("brain fog"), post-exertion malaise, and pain."`

These statements regarding "fatigue" do not convey the seriousness of the disease. Post-exertional malaise (PEM) should be a focal point of discussion. When the FDA asked ME/CFS patients to describe their disease, they did not say "fatigue." Patients told FDA that post-exertional malaise (PEM) was the most significant symptom: "complete exhaustion, inability to get out of bed to eat, intense physical pain (including muscle soreness), incoherency, blacking out and memory loss, and flu-like symptoms."

Multiple studies have demonstrated that patients with PEM have impairment in energy metabolism and lowered anaerobic threshold, and have shown that patients with depression, deconditioning and a number of other chronic illnesses do not have this kind of impairment.

3. Lines 6-7, "ME/CFS is an unmet public health need with an economic burden estimated to be greater than $1 billion."

The estimated economic impact to the U.S economy is from $18.7 to $24.0 billion annually in lost productivity and direct medical costs.

See: Jason, L., Benton, M., Valentine, L., Johnson, A., Torres-Harding, S., "The Economic Impact of ME/CFS: Individual and Societal Costs." Dynamic Medicine 2008, 7:6 doi:10.1186/1476-5918-7-6 http://www.dynamic-med.com/content/7/1/6.

4. Lines 63-64, "…limited research dollars directed at ME/CFS…" The Report should state that the level of funding for ME versus other serious illnesses is totally inadequate. The Report should emphasize that parity in NIH research funding with other serious diseases is essential to finding a cure for ME.

Based on NIH FY 2014 estimated funding for "Research, Condition, and Disease Categories" (RCDC) ME/CFS receives $5,000,000 funding; 1 million patients; $5 per individual patient

NIH support levels per patient for illnesses, which have a level of disability similar to ME, are as follows:

MS is funded at a level 57 times greater than ME. MS $115,000,000 funding; 400,000 patients; $287 per individual patient.

Lupus is funded at a level 13 times greater than ME. Lupus: $95,000,000 funding; 1.5 million patients; $63 per individual patient.

HIV/Aids is funded at a level 541 times greater than ME. HIV/Aids: $2,978,000,000 funding; 1.1 million patients; $2,707 per individual patient.

Cancer is funded at a level 18,683 times greater than ME. Cancer: $5,418,000,000 funding; 58,000 "current patients with cancer as primary diagnosis (2007)"; $93,413 per individual patient.

For FY 2014 NIH lists 237 Research/Disease Areas. Of the 237 areas three (3) receive zero funding and seven (7) receive funding of $5 million or less. Thus, of the 234 funded areas ninety-seven percent (97%) receive funding greater than the estimated $5 million support level for ME/CFS.

The Report should state that ME research funding demands serious review and correction by NIH leadership.

The Report should recommend drastically increasing NIH funding to cure ME/CFS.

As recommended by the Panel, this will include funding for innovative biomedical research; a bio-bank; a registry/repository; database for future investigations; multicenter studies; retrospective, prospective, and longitudinal studies; a central archive of data and tissue samples; clinical trials; a national and international research network; and bench-to-bedside policy research (Centers of Excellence).

In addition, the Report should specify that each area of funding, as recommended by the Panel, should be funded through a Request for Applications (RFA).

5. Significant NIH funding for biomedical research into the cause and cure of ME is essential. The lack of progress over the past thirty (30) years is directly attributable to the paltry dollar amount allocated by NIH to ME medical research.

Unfortunately, there is a Catch 22 involving NIH. NIH claims that they do not receive enough proposals for ME/CFS funding. Thus, they fund at a woefully low amount of $5 million. Researchers, on the other hand, think it is not worth applying since so little NIH money is available. For FY 2014 the estimated funding by NIH for ME/CFS research is $5 million.

NIH leadership must act responsibly and appropriately fund ME biomedical research. I urge the Panel to specifically address this problem in their Report.

In order to achieve research funding parity with other illnesses of similar severity and disability, what is the minimum annual amount that NIH should appropriate to ME? I do not presume to know. It is an important question, however, that I believe needs to be addressed in the Report.

As a starting point, I believe it is reasonable to suggest that NIH research funding for ME should be at least comparable, on a per patient basis, as Multiple Sclerosis (MS) which is considered to be an illness of similar severity and disability.

As explained above in item 4, MS is funded at $287 per individual patient. Thus, with one million patients, NIH should fund ME biomedical research at $287,000,000 or more.

It is essential that the Report discuss in detail the dire need for a significant increase in dedicated NIH research funding for ME.

The funding must be sufficient to implement all recommendations made in your Report including an aggressive program of biomedical research into the cause, treatment, and cure of ME.

6. Lines 68-70, "Patients usually have to make extraordinary efforts…to find a physician who will correctly diagnose and treat ME/CFS symptoms."

Lines 142-143, "Many patients are misdiagnosed and treated erroneously with potentially toxic therapies that may cause harm and diminish hope."

To correct this situation, the Report should recommend that NIH create a sufficient number of "Centers of Excellence" throughout the country to serve the one million ME/CFS patients.

The Chronic Fatigue Syndrome Advisory Committee (CFSAC) has repeatedly recommended the creation of "Centers of Excellence", but the recommendations have not been acted upon.

7. Lines 307-308, need to engage with "Health professional licensing and accreditation agencies to ensure a curriculum that facilitates ME/CFS knowledge acquisition."

The Report should state that medical schools and physicians' continuing education programs must adequately train medical students and physicians to diagnose and treat ME/CFS. The Report should also discuss the critical need to encourage more physicians to specialize in treating ME/CFS patients.

8. Lines 76-77, "Over the last 20 years, minimal progress has been made to improve the state of the science for patients with ME/CFS. Since the Incline Village, NV outbreak occurred in 1984, I suggest that the time period be changed to thirty (30) years or more.

The Report should recommend that NIH attempt to rectify the thirty years of "minimal progress" by fast-tracking research and funding to develop a cure for ME.

9. Lines 214-218, "The NIH Institutes and Centers … and other U.S. Department of Health and Human Services (HHS) agencies should coordinate research efforts to promote efficiency and effectiveness…"

Some endeavors are best accomplished through the collective resources of the Federal government. ME research is, I believe, in this category.

The Report should clearly place the responsibility on NIH to be pro-active in solving the ME/CFS public health issue. NIH must assume the overall responsibility to coordinate and fund research efforts to cure ME/CFS.

In order to best accomplish this, I believe the Report should recommend that either the National Institute of Neurological Disorders and Stroke (NINDS) or the National Institute of Allergy and Infectious Diseases (NIAID) assume responsibility for ME research.

ME needs to be associated with an NIH Institute that fosters biomedical research.

As previously explained in item 1 above, both HHS and NIH have failed in addressing the research and treatment needs of ME over the past thirty (30) years. Neither the Office of Women's Health (OWH) at HHS nor the Office of Research on Women's Health (ORWH) at NIH are disease researching entities. ME needs to be part of a biomedical research Institute at NIH.

10. Line 105, "A clear case definition…" and Lines 202-205, "Assemble a team of stakeholders…to reach consensus on the definition and parameters of ME/CFS."

The 2003 Canadian Consensus Criteria (CCC) has been adopted by expert researchers and clinicians. Although it may be improved upon, it is a valid starting point. The Report should recommend that NIH adopt the Canadian Consensus Criteria.

11. Line 5, "mostly women" and Lines 51-52, "…a research focus on men limits the applicability of current studies." and Lines 88-89, "Clinical studies have focused on predominantly Caucasian, middle-aged women." These statements seem to conflict. I question the accuracy of stating that there is a research focus on men regarding ME/CFS.

12. Lines 365-366, "Thus, for needed progress to occur we recommend (1) that the Oxford definition be retired…" I suggest that you also recommend the retirement of the Fukuda definition.

13. Lines 113-114, "Existing treatment studies (cognitive behavioral therapy (CBT) and graded exercise therapy (GET) demonstrate measurable improvement…." I disagree. Without the Oxford definition and the PACE trial, there is little evidence to support either CBT or GET.

14. Lines 234-235, "Research is needed investigating the effect of the intestinal microbiome on ME/CFS…." I suggest also recommending further research on the autonomic nervous system.

15. Line 350, "Future treatment studies should evaluate multimodal therapies." It is my understanding that multimodal therapies have been tried and found ineffective in Sweden.

16. Lines 351-352, "We recommend that NIH and the FDA convene a meeting on the state of ME/CFS treatment." Would the purpose of this meeting be different than the 2013 FDA meeting on drug development for ME/CFS? If so, what would it be?

17. Omission: I do not believe the Report recommends research regarding pediatric ME patients. I believe it is important to understand the differences and/or similarities in the onset and progression of ME between children/adolescents and adults. In addition, children and adolescents with ME often have great difficulty continuing their education. Information and support on the best approaches to allow them to continue in school should also be addressed.