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**Sponsored by:**Trans-NIH ME/CFS Research Working Group Office for Research on Women's Health (ORWH) Office of Disease Prevention (ODP) National Institutes of Health (NIH)

### **Summary**

On December 9-10, 2014, the National Institutes of Health (NIH) held

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agencies, patient advocacy groups, and patients and their families, have a shared responsibility for meeting the needs described herein, and thereby improving the lives of people living with ME/CFS.

#### **Background**

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a chronic, complex, and multifaceted disease characterized by substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities; post-exertional malaise; unrefreshing sleep; and at least one of the prepared a report summarizing the meeting

(https://prevention.nih.gov/docs/program s/mecfs/ODP-P2P-MECFS-FinalReport.pdf). The P2P panel identified research gaps and future research priorities, and made seven recommendations directed toward federal and non-federal agencies, vendors, health care systems, and clinicians (Green et al., 2015).

On May 24, 2016, government representatives (hereafter called the "federal partners") met to develop approaches to address the recommendations outlined in the panel report on Advancing the Research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. The objectives of the Federal Partners Meeting were to identify opportunities to leverage existing resources and promote collaboration and synergy, while reducing overlapping efforts across the federal agencies, with the ultimate goal of generating rigorous scientific evidence that can lead to improved care for individuals with ME/CFS.

This report summarizes the discussions from the Federal Partners Meeting (see Appendix for a list of participants), which focused on the P2P panel's recommendations:

- 1. Define disease parameters.
- 2. Create new knowledge about ME/CFS.
- 3. Improve methods and measures used in ME/CFS research.
- 4. Provide training on and education about ME/CFS.
- 5. Identify new funding resources.

- 6. Conduct clinical trials.
- 7. Improve treatment.

An analysis of research activities or initiatives conducted or supported by the participating federal agencies relevant to these recommendations contributed to the discussion of research and programmatic gaps, as well as the opportunities for collaboration. Participants considered the areas for collaboration that should be given the highest priority and the resources that could be utilized to address these areas.

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# **Summary of Discussion of P2P Panel Recommendation I: Define Disease Parameters**

Background: The P2P panel report identified the lack of a specific and sensitive diagnostic test and clearly defined diagnostic criteria as key impediments to ME/CFS research.
Fatigue, long considered the defining feature of ME/CFS, does not fully capture the complexity of the disease, treatment response, or the experience of individuals with ME/CFS. While a number of diagnostic criteria are in use—CDC (Holmes et al., 1988), Fukuda (Straus et al., 1994), International (Carruthers et al., 2011), Canadian (Carruthers et al., 2003), and the IOM criteria (Institute of Medicine 2015)—none is uniformly recognized as the diagnostic standard.

**Specific Research Focus Areas:** One key area where federal partners may help in better defining ME/CFS is the translation of clinical diagnostic criteria into criteria for research studies. To achieve this, the federal partners discussed:

 The methods and research that are required to identify the underlying cause(s) of ME/CFS. When research leads to a biomarker and/or identifies the cause(s) of ME/CFS, then an objective definition of ME/CFS can be created, along with a clinical diagnostic test. The absence of a standard case definition and lack of consensus in the community about which one to use for clinical studies of ME/CFS leads to confusion and the inability to draw correlations across studies that use different definitions. It is agreed that such features as the heterogeneity of symptoms and the specific quality of the fatigue (i.e., postexertional malaise) need to be taken into account in all studies of ME/CFS. Clinical criteria outlined in the **Institute of** Medicine's recent report on ME/CFS should inform these efforts. Discussants acknowledged that more research is needed before a case definition can be established. Involvement of individuals with ME/CFS and health care providers in defining both disease parameters and outcome measures will lead to optimal results.

 The information contained in the <u>FDA guidance for industry on</u> <u>developing drugs for ME/CFS (April</u> <u>2013)</u> was developed to advance the regulatory science to support clinical outcome assessment for ME/CFS, and can help to guide future ME/CFS research efforts.

## Opportunities for Collaboration Among Federal Agencies, Resource Development, and Next Steps:

Several opportunities for federal partner collaboration in supporting activities and research that may lead to an improved definition of ME/CFS were identified:

 Develop Common Data Elements (CDEs) for ME/CFS. CDEs will allow researchers and clinicians to standardize the collection of data in order to facilitate comparison of results across studies and more effectively aggregate information into significant metadata results. The NINDS Common Data Elements Project can serve as a guide for the development of CDEs for ME/CFS. This process will take advantage of existing resources in the community (the CDC-funded Multi-site Clinical Assessment of CFS study), as well as at NIH [Patient-Reported **Outcomes Measurement Information** System (PROMIS), the NIH ToolBox, OMERACT, and the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network].

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- Community-based participatory research and patient reported outcome (PRO) measures offer opportunities for capturing the assessment of symptoms and function by individuals with ME/CFS.
- Future studies could take advantage of emerging technologies, such as telemedicine, in order to reach homeand bed-bound individuals with ME/CFS.

# Summary of Discussion of P2P Panel Recommendation II: Create New Knowledge

**Background:** Studies of ME/CFS are fraught with methodological problems, preventing a clear understanding of who is affected by ME/CFS: there are no universally agreed-upon parameters for defining ME/CFS, no accurate ways of identifying and diagnosing ME/CFS and, as one participant pointed out, 163 possible combinations of symptoms associated with the disease. In addition, small

limits generalizing the results of current studies. Some instruments used to evaluate ME/CFS are not validated, are inappropriate, and may be misleading. All of these issues contribute to inconclusive research results and a lack of definitive knowledge about incidence, prevalence and potential causes and treatments (Green et al., 2015).

**Specific Research Focus Areas:** The following research priorities were identified by the federal partners:

 Invest in bench-to-bedside research. Research that provides detailed analysis of multiple measures in large numbers of individuals with ME/CFS would help investigators to intermediately ander the

Through a contract with the Center for Advanced Professional Education, the CDC developed a set of videos for the MedEdPORTAL focusing on the doctor-patient interaction and pediatric/adolescent ME/CFS. This resource could be expanded to include additional ME/CFS materials. It would be important also to develop educational materials for other health care providers including nurses, physician assistants, etc.

**Developing educational materials** with broad stakeholder collaboration: Individuals with ME/CFS, advocates, medical professional and educational organizations, clinicians with expertise in ME/CFS, and government (HHS ex offici6FSAC members) could work together to develop educational materials. One way to foster collaboration between academic centers and the federal government is to identify grants and funding opportunities for development of educational programs and materials for health care professionals and for individuals with ME/CFS and their caregivers.

## Opportunities for Collaboration Among Federal Agencies, Resource Development, and Next Steps:

Developing ME/CFS educational materials offers several collaborative opportunities:

 Working together on educational materials would help promote communication among stakeholders and improve dissemination of educational materials to the health care provider community.  Educational materials should incorporate the recommendations from the IOM ME/CFS report.

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- Topic/delivery method needs for continuing medical education (CME) resources should be assessed as they relate to ME/CFS.
- Educational materials should communicate consistent messages and the federal partners should present accurate, evidence-based, and up-to-date information on ME/CFS.
- Stakeholders should partner on agencydeveloped CME courses and reach out to primary care providers to promote these resources. The optimal outreach strategy will need to be determined.
- The HHS Health Resources & Services
   Administration (HRSA) supports
   community health centers that seat sen agey cd







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