Public Comment

Mary Dimmock

Good morning. Thank you for the opportunity to talk to you today.

First, I wish to thank the FDA for creating an opportunity that has never been seen before in this patient community – a true glimpse into the devastation of this disease and greater clarity on the steps that need to be taken. This is an opportunity that we must not squander.

I also want to thank all the patients who attended, submitted comments to the docket, participated by teleconference, and discussed it on the forums. Your testimony and participation made the difference. Light bulbs went off and people began to see how hellish this disease is.

But beyond that, the biggest lesson to me is an old lesson – we are not going anywhere until we address the fundamentals. First, fix the definition. Second, provide research funding commensurate with disease burden and use it to validate biomarkers and outcome measures and execute the preliminary clinical trials to encourage pharmaceutical investment.

The first issue is the definition: A group of patient organizations and advocates recently sent a letter sent to Secretary Sebelius, Dr. Frieden, Dr. Collins and Dr. Koh calling for the adoption of the Canadian Consensus Criteria and stopping the use of non-specific definitions and medical education material associated with CFS. The main letter and the link to the full position paper are included in this testimony.

We have taken that position because we believe that resolving the current confusion around the nature of this disease is essential to forward progress. Currently, the CDC defines CFS through an apples and oranges collection of "CFS" definitions. Three require the hallmark symptoms of ME but the two most commonly used, Fukuda and Oxford, do not require hallmark symptoms, allow primary psychiatric illness and in the case of Oxford only requires one symptom – 6 months of disabling fatigue. This has created tremendous confusion by associating ME with depression, deconditioning, excessive rest, maladaptive coping styles, false illness beliefs and a catchall for any unexplained chronic fatigue. The confusion has confounded research with conflicting results, stalled drug development and negatively impacted clinical care. Patients have paid the price with harmful recommendations, stigma and disbelief – and a lack of treatments.

Remember the patients from the FDA. Those patients do not suffer from deconditioning, false illness beliefs or maladaptive coping. They suffer from a devastating disease that has stolen their lives and left them at the mercy of a body that has fallen apart. We must stop the confusion about this disease. We must adopt Canadian Consensus Criteria as a definition that appropriately describes this disease.

The second issue from the FDA meeting was the need for research to validate outcome measures, agree to biomarkers and perform the initial clinical trials of promising treatments. And that is going to require money – money has not been committed to date. In 2012, NIH spent $4.5M on the CFS program. And of that $4.5M, it's questionable whether $822K was really for

CFS[1] leaving $3.7M in total funding. At that level, funding for CFS is #225 out of 235 disease funding and just 3 percent of the funding for multiple sclerosis, a disease with a similar level of disease burden.

We are told that the science isn't ready yet, that researchers are not interested, that good proposals are not being submitted, that NIH doesn't fund some of the needed studies. But we hear our best researchers trying and failing to get NIH grants for biomarkers, outcome measures, clinical trials for a number of promising treatments like Rituximab and anti-virals, and genetics. We have seen a number of private institutes put in place. We see similar studies being funded for other diseases. This isn't lack of interest but a lack of committed funding and what from the outside appears to be a problem in getting this disease prioritized within NIH institutes focused on their own priorities.

We are also told that we have shrinking budgets as though that explains the failure to provide a fair share of funding. We understand the challenges of sequestration and tight budgets. But we are asking for NIH to do what CFSAC has recommended over the years - provide a level of funding that is commensurate with the significant burden of this disease. We are asking for what Dr. Klimas asked Dr. Clayton for in the November 2011 CFSAC – to work through whatever barriers have starved research into this disease for so many years. We are asking for what is so clearly needed to fuel drug development - biomarkers, outcome measures, characterizing the subtypes to aid clinical trial design and execute initial clinical trials to encourage pharmaceutical investment.

The challenges we face are significant and have been decades in the making. But the opportunities to change the future are palpable. For their part, patients are committed to collaborating to find solutions. But with all due respect to Mr. Munos at the FDA meeting, they are too stigmatized, impoverished and terribly ill to come up with the funding to solve these challenges on their own. They already pay for this disease with their lives and with $18-23B a year in lost productivity and direct medical costs. If there ever was a time for the NIH to step up to the plate, it is now. Do not let this opportunity go by. Provide funding to match the disease burden and get the needed studies done.

Thank you

1) The following three grants do not appear to be specifically related to CFS or ME

- http://projectreporter.nih.gov/project_info_description.cfm?projectnumber=1R03DK093874-01 ($80K)
- http://projectreporter.nih.gov/project_info_description.cfm?projectnumber=5R01GM070837-07 ($293K)
- http://projectreporter.nih.gov/project_info_description.cfm?projectnumber=1ZIAAI000058-38 ($449K)

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The following is the main body of the letter that was sent to Secretary Sebelius, Dr. Frieden, Dr. Collins and Dr. Koh calling for the adoption of the Canadian Consensus Criteria and stopping the use of non-specific CFS definitions and medical education material. The full position paper can be found at this link: http://bit.ly/YDPnmJ

Date: May 12, 2013
To: Secretary Sebelius, Dr. Howard Koh, Dr. Thomas Frieden, Dr. Francis Collins
CC: Dr. Janet Woodcock, Dr. Beth Unger, Dr. Susan Maier, Dr. Nancy Lee, CFSAC
Subject: Need for Focused Attention on Myalgic Encephalomyelitis (ME)

Dear Secretary Sebelius, Dr. Koh, Dr. Friedan, and Dr. Collins:

We are writing to express our strong concerns with the Department of Health and Human Services (DHHS) current definition activities related to "Chronic Fatigue Syndrome" ("CFS"). We believe DHHS is moving in a direction that is unproductive and harmful to patients. This letter outlines the basis for these concerns and the steps we believe must be taken to rectify the situation.

Throughout the twentieth century, there have been occurrences of a complex, disabling disease characterized by unrefreshing sleep, flu-like symptoms, impairment of memory and other cognitive impairments, orthostatic intolerance, debilitating weakness, pain, fever and the hallmark symptom of post-exertional malaise (post-exertional neuroimmune exhaustion). This disease has been shown to cause severe dysfunction of neurological, immune, endocrine and energy production systems and, since 1969, has been classified as a neurological disease called myalgic *encephalomyelitis* (ME) by the World Health Organization. The name myalgic *encephalomyelitis* is still used elsewhere and is used herein to refer to this disease and to clearly distinguish it from the non-specific term "CFS".

Following the outbreak in Incline Village, the CDC named the disease chronic fatigue syndrome (CFS) instead of myalgic *encephalomyelitis* and developed the first of a number of fatigue-focused case definitions. Today, the term "ME" is rarely used in the U.S. and instead, ME patients are almost always given a diagnosis of CFS.

Unfortunately, according to the CDC website, "CFS" can be defined by at least 5 disparate CFS definitions (see Table 1). Three of these, the 2003 Canadian Consensus Criteria, the 2011 ME International Consensus Criteria, and the Pediatric definition, describe the essential and hallmark features of ME. But the two most commonly used definitions, the 1994 Fukuda and 1991 Oxford definitions, focus on fatigue, do not require core ME symptoms like post-exertional malaise, cognitive problems and unrefreshing sleep and allow the inclusion of primary psychiatric illness. In fact, Oxford does not require any symptoms except for 6 months of disabling fatigue for a patient to be given a diagnosis of CFS.

As a result, the term "CFS" has become an amorphous umbrella associated with a diverse set of unrelated conditions that include depression, deconditioning, medically unexplained chronic fatigue, school phobia, and for some researchers and clinicians, fatigue due to "excessive rest" or "false illness beliefs". In clinical practice, doctors give a CFS diagnosis to a heterogeneous mix

of patients – those with ME, those with the varied conditions listed above, those who have been misdiagnosed or those whose doctors use CFS as a catchall diagnosis for fatigue.

ME is unquestionably a complex disease and its heterogeneity is real. But this "heterogeneity" is a manufactured artifact of the amalgamation of diverse definitions and unrelated patient populations into one clinical entity called "CFS". Tragically for ME patients, this has obscured ME in a "web of confusion", which has confounded ME research, virtually precluded drug development and resulted in widely divergent prevalence estimates. This confusion has also negatively impacted clinical care, led to inappropriate and sometimes harmful "one size fits all" clinical guidelines applied to all "CFS" patients and created a climate in which physicians routinely dismiss ME as not real or not serious.

There is an urgent need to stop perpetuating this confusion and start researching and treating the disease that these patients actually have – myalgic encephalomyelitis.

Given the current embrace of these non-specific "CFS" definitions and the failure to directly engage ME patients and ME experts in the current DHHS definition initiatives, we believe that the outcome of these DHHS initiatives will further exacerbate an already intolerable situation.

The following steps are necessary in order to move forward with improved research and treatment for patients with ME:

1. **Adopt a disease appropriate case definition:** ME, as defined by the Canadian Consensus Criteria (CCC), must be recognized by DHHS and the United States government for the serious and debilitating disease that it is. ME is not a subtype of "CFS". The CCC must be adopted now as the baseline case definition for this disease. It can be evolved as additional knowledge is gained, the definition is operationalized and markers are validated. We do not need more years of study to fix what is so clearly broken today.

2. **Stop using "CFS":** The terms "Chronic Fatigue Syndrome" and "CFS" must be permanently abandoned along with the overly broad, two-decades old Fukuda and Oxford definitions. By using non-specific criteria that have become associated with such a diverse set of unrelated conditions, these terms and the accompanying definitions have become medically and scientifically meaningless. They are impeding forward progress and DHHS should discontinue their use. DHHS should also discontinue the dissemination of "CFS" clinical information, like the 'one size fits all' CDC CFS Toolkit, that uses a non-specific disease description and includes clinical findings and recommendations for all patients based on Oxford, Empirical or chronic fatigue studies.

3. **Manage the transition to the Canadian Consensus Criteria:** This includes the adoption and proactive dissemination of appropriate medical guidance like the International Association for CFS/ME Primer, available through DHHS' Guidelines.gov. It also includes the establishment of a research program focused on ME, updated insurance guidelines for Medicare/Medicaid, the establishment of disability guidelines for

ME and similar transition activities. Most importantly, it must include a plan to care for those patients who have received a diagnosis of "CFS" but do not meet the CCC criteria for ME. These individuals should be properly evaluated and diagnosed where possible. If unexplained conditions remain, additional studies will be needed to understand these conditions and establish more appropriate names and definitions. The continued use of the overly broad "CFS" and Fukuda for these patients is not appropriate.

4. **Engage ME stakeholders in the planning and implementation:** In keeping with President Obama's commitment to Open Government, the key stakeholders – ME patients and ME experts – must be engaged in a full and open partnership to plan for and ensure implementation of this change. We are the ones that best understand this disease and will provide valuable input to these activities.

For decades, ME patients have borne the brunt of the failure to correct the flaws with how "CFS" has been defined. We will not accept this situation any longer.

The FDA Stakeholder Workshop has provided a unique opportunity to approach this disease in new ways, starting with the definition. It is time to adopt the Canadian Consensus Criteria as the baseline case definition for ME research and clinical care and move forward from there. Doing so will energize the wheels of research and drug development and begin to directly improve the lives of the many Americans stricken with this devastating disease.

We look forward to partnering with you to make this a reality for patients. We respectfully request a response to our concerns along with an explanation of how ME patients and ME experts will be engaged in this process by June 5, 2013. Do not hesitate to contact us if you need additional information.

Thank you.

Signed Patient Organizations

Chronic Fatigue Syndrome, Fibromyalgia and Chemical Sensitivity Coalition of Chicago	The Fibromyalgia-ME/CFS Support Center, Inc.
CFS/Fibromyalgia Organization of Georgia, Inc.	Rocky Mountain CFS/ME and FM Association
MAME (Mothers Against Myalgic Encephalomyelitis)	Speak Up About ME
PANDORA (a.k.a. CFS Solutions of West Michigan)	Wisconsin ME/CFS Association, Inc.
Phoenix Rising	

Independent Patient Advocates

Bobbi Ausubel	Suzan Jackson	Justin Reilly, J.D.
Rich Carson	Jill Justiss	Mary Schweitzer, Ph.D.
Lori Chapo-Kroger, R.N.	Mindy Kitei	Meghan Shannon MS MFT
Kati Debelic, R.N.	Michele Krisko	Marly Silverman
Mary Dimmock	Denise Lopez-Majano	Rivka Solomon
Pat Fero, MEPD	Mike Munoz	Tamara Staples
Joan Grobstein, M.D.	Matina Nicolson	Charlotte von Salis, J.D.
Jean Harrison	Donna Pearson	Michael Walzer
Eileen Holderman	Leela Play	