The Twentieth Meeting of
THE CHRONIC FATIGUE SYNDROME
ADVISORY COMMITTEE
US DEPARTMENT OF HEALTH AND HUMAN SERVICES

Holiday Inn, Columbia Room, 550 C Street, SW
Washington, DC 20024
Wednesday, November 9, 2011 – 9:00 am to 4:30 pm

Voting Membership

Name		Term
Chairman Christopher R. Snell, PhD	**Stockton, CA**	**04/01/07 to 04/01/12**
Dane B. Cook, PhD	**Madison, WI**	**05/10/10 to 05/10/14**
Jordan D. Dimitrakoff, MD, PhD	**Boston, MA**	**05/10/10 to 05/10/14**
Eileen Holderman	**Galveston, TX**	**05/10/10 to 05/10/14**
Michael Houghton, PhD	**Danville, CA**	**05/10/10 to 05/10/14**
Leonard Jason, PhD	**Chicago, IL**	**04/01/07 to 04/01/12**
Steven P. Krafchick, MPH, JD	**Seattle, WA**	**07/01/10 to 07/01/14**
Nancy Klimas, MD	**Miami, FL**	**04/01/07 to 04/01/12**
Susan M. Levine, MD	**New York, NY**	**05/10/10 to 05/10/14**
Gailen D. Marshall Jr., MD, PhD	**Jackson, MS**	**05/10/10 to 05/10/14**
Ann Vincent, MD	**Rochester, MN**	**04/10/11 to 04/10/15**

Ex Officio Membership

Agency for Health Research and Quality
Beth A. Collins Sharp, PhD, RN
Senior Advisor for Women's Health
and Gender Research

Centers for Disease Control and Prevention
Ermias Belay, MD
Associate Director for Epidemiologic Science
Division of High-Consequence Pathogens

Center for Medicare and Medicaid Services
Alaine Perry, MPH
Senior Advisor for Disability
and Special Need Population
CMS Center for Strategic Planning

Food and Drug Administration
Theresa Michele, MD
Medical Officer Team Leader
Center for Drug Evaluation and Research

Health Resources and Services Administration
Deborah Willis-Fillinger, MD
Senior Medical Advisor
HIV/AIDS Bureau

National Institutes of Health

Primary
Charles Wells, PhD
Senior Advisor
Office of Research on Women's Health
Office of the Director

Alternate
Janine Austin Clayton, MD
Deputy Director
Office of Research on Women's Health
Office of the Director

Social Security Administration

Primary
Cheryl A. Williams
Director
Office of Medical Listings Improvement

Alternate
Michele Schaefer
Acting Deputy Director
Office of Medical Listings Improvement

Designated Federal Officer
Nancy C. Lee, MD
Deputy Assistant Secretary for Women's Health

Alternate Designated Federal Officer
Martha D. Bond
Senior Public Health Advisor
Office on Women's Health

Agenda

9:00 a.m.	**Call to Order** **Opening Remarks**	pg	Dr. Christopher Snell, PhD *Chair, CFSAC*
	Roll Call, Housekeeping	pg	Dr. Nancy Lee, MD *Designated Federal Officer*
9:15 a.m.	**HHS Office on Disability**	pg	Rosaly Correa-de-Araujo, MD, MSc, PhD *Deputy Director* DHHS Office on Disability
10:00 a.m.	**Centers for Disease Control and Prevention Web Page**	pg	Eileen Holderman; Nancy G. Klimas, MD; Ermias Belay, MD
10:30 a.m.	**Break**	pg	
10:45 a.m.	**Agency Updates: CDC, SSA, NIH**	pg	*Ex Officio* Members
11:45 a.m.	**Minimal Elements for Papers**	pg	Leonard A. Jason, PhD
12: 15 p.m.	**Subcommittee Lunch**	pg	Subcommittee Members
1:15 p.m.	**Public Comment**	pg	Public
2:15 p.m.	**Break**	pg	

2:30 p.m.	**Committee Discussion** **Finalize Recommendations**	pg	Committee Members
4:30 p.m.	**Adjourn**	pg	

Opening Remarks

Dr. Snell called the meeting to order and waived opening remarks.

Roll Call

Voting Members:

Dr. Dane B. Cook, Assistant Professor of Kinesiology, University of Wisconsin-Madison, researching exercise and functional brain imaging in chronic fatigue syndrome (CFS).

Mr. Steven P. Krafchick, attorney representing CFS patients, specializing in helping them receive long-term disability benefits from private policies.

Dr. Ann Vincent, general internist at the Mayo Clinic with a research interest in CFS and fibromyalgia.

Dr. Leonard Jason, psychologist at DePaul University, with an interest in CFS diagnostic issues, epidemiology, and case definition.

Dr. Susan M. Levine, physician treating CFS and fibromyalgia patients in New York City.

Dr. Christopher Snell, CFSAC Chair and Professor, University of the Pacific in Stockton, California, with an interest in functional aspects of CFS.

Dr. Nancy Klimas, University of Miami, investigator and clinician who cares for patients with CFS.

Dr. Gailen Marshall, University of Mississippi, a clinical immunologist interested in biomarkers for CFS.

Dr. Jordan Dimitrakoff, Harvard Medical School, studying chronic pelvic pain syndrome, interstitial cystitis, and their relationship with CFS.

Eileen Holderman, CFS patient advocate.

***Ex Officio* Members:**

Dr. Theresa Michele, Food and Drug Administration (FDA)

Dr. Beth Collins Sharp, Agency for Healthcare and Research Quality (AHRQ)

Alaine Perry, Center for Medicare and Medicaid Services (CMS)

Dr. Ermias Belay, the Centers for Disease Control and Prevention (CDC)

Ms. Michele Schaefer, Social Security Administration (SSA)

CFSAC Staff:

Dr. Nancy Lee, Designated Federal Officer (DFO)
Ms. Martha Bond, Alternate DFO

Others:

Elizabeth Unger, MD, PhD, *Chief*, Chronic Viral Diseases Branch, CDC

Absent from Roll Call: CFSAC voting member **Dr. Michael Houghton** and *ex officio* members **Dr. Deborah Willis-Fillinger**, Health Resources and Services Administration (HRSA); and **Dr. Charles Wells**, National Institutes of Health (NIH). These *ex officio* members joined the meeting at a later time.

Housekeeping

Dr. Lee addressed several housekeeping items:

- Explained the procedure for CFSAC members to order and pick up their lunch.
- As a first-time DFO, thanked CFSAC members and the public for an informative meeting the previous day at which she learned a lot about CFSAC committee procedures and the field of CFS.
- Reiterated what CFSAC is intending to do over the next few months to make meetings a smoother process:

- Establish a listserv. The sign-up procedure will be posted on the CFSAC website. Those who sign up will receive information at the same time as it is posted on the website. The process will be handled by the communications staff within Office of Women's Health (OWH).

- Improve the CFSAC website, which is dull and user unfriendly. The intention, however, is not to make the CFSAC website *the* go-to place for CFS. OWH does not have the necessary expertise. The CFSAC site will be a more user friendly resource for people who want to learn what is happening with the committee.

- Bring on Chris Williams as a part-time contractor with CFSAC. She will be a liaison to the advocate community and help CFSAC members understand more about scientific and patient issues.

- Update the CFSAC charter and bylaws in 2012, as required by law every two years. Committee staff will be talking to CFSAC members to get their input. Dr. Lee noted that she serves as an *ex officio* on an advisory committee that includes non-voting liaison representatives from non-governmental organizations related to that health concern. She is looking into having such representatives on CFSAC. It would require a charter change. The new charter has to be in

place by September 2012. The process will take until at least the fall CFSAC meeting and may take longer. Dr. Lee asked for patience from interested parties.

- Provide a live audio feed of the CFSAC meeting, then a posting of a complete 508-compliant video of the meeting within a week. Dr. Lee explained that DHHS is under very severe budget constraints which could become worse depending on end-of-year Congressional budget action. OWH has had to cancel all staff travel for the rest of 2011 due to lack of funding. CFSAC has made the decision not to provide live video streaming of the meeting on the internet because the cost has gone up significantly since live streaming was instituted. The May 2011 live meeting stream was incredibly expensive and CFSAC can no longer afford it. Committee staff will continue to look into other cost-effective technologies and are hoping to find a way to increase accessibility by the spring 2012 meeting.

- Continue to hold meetings in a hotel venue. Dr. Lee noted that the larger room more comfortably accommodates movement and spares attendees from having to cope with security measures. She asked for feedback via the CFSAC website.

- Dr. Lee asked that all CFSAC members give their name before making comments to better accommodate those listening to the live audio stream. She asked Dr. Snell to recognize those who speak by name.

- Dr. Lee thanked Deborah Eby for producing the meeting minutes; the NIH film crew; Seamon Corporation and Conference Planner Brittany Irvine; and the team from the Office on Women's Health: Joyce Grayson, Emmett Nixon, Ursuline Singleton, and Martha Bond.

Dr. Snell explained that when CFSAC began looking into the international classification of diseases, it found that there was also an international classification for functionality disability and health. He introduced Dr. Rosaly Correa-de-Araujo to discuss how ICF might work for CFS.

International Classification of Functioning, Disability, and Health: Application and Relevance to Chronic Fatigue Syndrome

Rosaly Correa-de-Araujo, MD, MSc, PhD, *Deputy Director*, Office on Disability, DHHS

The International Classification of Functioning, Disability, and Health (ICF) was developed by the World Health Organization (WHO) and approved in May 2001 by the World Health Assembly. The ICF is a multi-purpose classification designed to provide a standard language and framework for the description of two domains: health and health-related states. These domains are described from the perspective of the body, the individual, and the society.

The ICF systematically groups different domains or areas within domains for a person with a health condition. If a person has a specific disease or illness, the ICF looks into what the person can do with that condition.

Functioning encompasses all body functions and structures, activities, and participation. Disability relates to impairments, body functions and structure, limitations to activities, or restrictions in

participation in certain activities or in the environment where the person lives. There would also be environmental factors and personal factors that affect all of those categories or domains.

Sample Case – International Classification of Disease (using ICD-9 coding)

Ms. Harris and Ms. Brown are both 52 year old females with a history of multiple sclerosis with a relapsing remitting course who are both dependent on others for activities of living (ADL). The ICD-9 code is 340-multiple sclerosis.

Although the situation for the two individuals appears similar, they are very different when one goes deeper and takes the medical history. Both have the same diagnosis, but a very different functioning profile. Ms. Harris uses a power wheelchair while Ms. Brown is unable to speak or eat. They have a completely different functional status.

When the medical history is collected using ICF, one can code the difficulties with dressing (d540.44); with moving (d460.14); with acquiring, keeping, and terminating a job (d845.0, d845.4); and even issues related to the parenting relationship (d7600.0, d7600.4). In this example, Ms. Harris was a successful parent while Ms. Brown has a daughter but cannot take care of her. It is important to be able to identify and code in a way that will be understood by everybody.

ICF Structure

ICF has two parts: Part 1 – Functioning and Disability and Part 2 – Contextual Factors. Each part consists of various domains. Within each domain are categories, which are considered to be the units of the classifications. The health and health-related states of a person can be recorded by selecting the appropriate category under the two parts. One can also add qualifiers to those codes.

Part 1 domains are Body Functions (b), Body Structures (s), and Activities and Participation (d).
Part 2 domains are Environmental Factors (e) and Personal Factors.

We have codes for each of these domains, and then we qualify them.

Part 1 – Functioning & Disability

Body Functions & Body Structures

Body Functions can be physiological and psychological.
Body Structures refer to the anatomical parts of the body.
Impairments are problems in the body function and/or the body structures. They could represent a significant loss of function.

The body functions mirror the body structures. For example, seeing is related to the eye and all eye-related structures. The body functions and structures also have to correlate with body systems.

Activities & Participation

When one thinks about Activities and Participation under Part 1 – Functioning & Disability:

- Activity is the execution of a task or action by an individual.
- A limitation is a problem in executing a task or activity.
- Participation is the involvement in a life situation.
- Restriction is a problem in participating in a life situation.
- Sometimes these four can overlap.

There are Chapters on Activities & Participation where the codes are found. Some chapter examples include: Learning & Applying Knowledge (1), Communication (3), Self Care (5), and Interpersonal Interactions (7).

Part 2 – Contextual Factors

Environmental Factors, a Contextual Factor, considered from the perspective of the person whose situation is being described. They can serve as Facilitators or Barriers. The chapters under Environmental Factors include:

- Products and technology that the person uses
- The natural environment and changes to the environment
- Support and relationships.
- Attitudes
- Services, systems, and policies

Qualifiers

The codes for domains, categories, and chapters are designed to be neutral. The qualifiers are important because they are ratings assigned to each of the codes. Qualifiers determine the meaning of a particular code when it is applied to a particular person. An example would be looking into a person's situation to evaluate the nature of a change. One would be coding that person with a specific condition. The qualifier to be used may:

- Indicate that there is an impairment for that particular person as it relates to a body part.
- Indicate if the problem is occurring on the left, or right, on the front, or on both sides of the body.
- Reflect performance (how people with a problem can live in the environment).
- Address the issue of capacity (what people do in the clinical setting).

The qualifiers are based on a severity scale that goes from NO problem (0) to a COMPLETE problem (4) as well as not specified (8) or not applicable to the condition (9). There is another scale for the environmental factors. The facilitators are marked with a plus sign before the rating. The facilitators for the environmental factors are mild, moderate, substantial, and complete.

Example of ICF basic coding dealing with the Body Function Qualifier: b3300.3

This represents a 32 year old woman presenting with a stuttering problem and severe difficulty with starting a sentence and transitioning from one word to another.

b=body function
3300=item code dealing with fluency of speech

3=the qualifier indicating that the condition is severe

The system is easily used to compare or evaluate data.

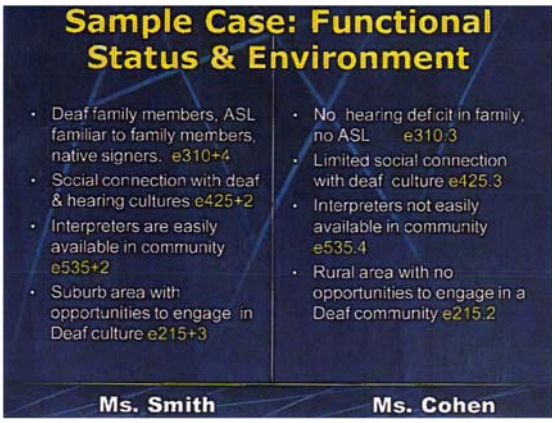
Another example: d4502.2189

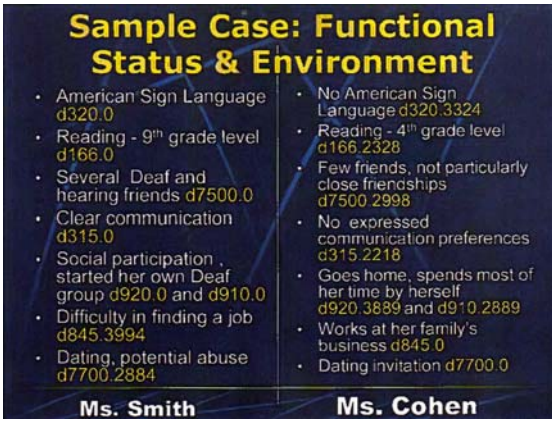
This represents a person with balance difficulty. The person has problems walking on different surfaces. The person is not able to perform her job in the way it would be expected of her.

d=activities and participation
4502=item code dealing with Walking on different surfaces
2=Qualifier 1 Current performance: moderate
1=Qualifier 2 Capacity without assistance: mild
8=Qualifier 3 Capacity with assistance: not specified
9=Qualifier 4 talking about Performance without assistance: not applicable

Sample Case: Functional Status & Environment

Ms. Smith and Ms. Cohen are both 16 year old deaf white females using hearing aids who are high school students living with family. The codes [referring to the first chart below] all begin with "d", which refers to Activities & Participation. The codes in the second chart below begin with "e" and are specifically related to the environment.





At a system level, ICF can do a lot. Codes and categories can provide a universal framework for needs assessment. When one assigns ratings to those codes, one can determine the depth and the breadth of the need according to the categories being used. One can also track a person's performance ability—the functional capacity—through use of relevant ICF codes and qualifiers. One can provide a record of change that may occur in the course of a condition or an intervention that a person may be submitted to. By assigning qualifiers to the ICF codes, one can examine the impact of different interventions across a range of functional categories.

For example, if person A receives a certain treatment because of a stroke and person B receives a different treatment for the same type of stroke, one looks at the codes to evaluate which intervention had the greater impact on functioning by determining the degree of change that has happened over time and how deep and broad that change is. Also, additional knowledge about functioning can indicate which individual who had the same ICD diagnosis would benefit from additional interventions. The ICF is

easy to incorporate into electronic health records because it is composed of alphanumeric codes and ratings. ICF coding would provide a lot of information to evaluate where the gaps are with numerous individuals and what else needs to be done.

ICF has not been adopted by the United States. Most of the work here so far has been done by The Washington Group on Disability Statistics formed in 2001 as a result of the United Nations Seminar on Measurement of Disability held in New York City. It was recognized at that time that statistical and methodological work was needed at an international level to facilitate cross-national data comparison on disability. The United Nations invited the NCHS/CDC to launch The Washington Group.

The group developed a set of questions for use on a national census for gathering information about limitations in basic activity functioning among national populations. Those questions have already been tested so they are ready for implementation everywhere in the world. Researchers will be able to compare populations that are living under different conditions and cultures. This is a major advancement.

The IOM Report

- In 2007, the Institute of Medicine (IOM) issued a report proposing to use the ICF the tool for classifying health status among Americans with disabilities in the U.S. health and social service systems. IOM concluded that NCHS/CDC, the US Census Bureau, the Bureau of Labor statistics, and other relevant government units involved in disability monitoring should adopt ICF as their conceptual framework. This also includes CMS, the Veterans Administration (VA), and the Social Security Administration (SSA).

- The IOM report pointed out weaknesses in the ICF system. The report recommended, for example, that quality of life and classifications for personal factors should be incorporated. The report also recommended incorporating secondary health conditions because they are important for people with disabilities.

- In the report's "Final Thoughts," the IOM states: "Evidence continues to grow that disability is not an unavoidable consequence of injury or chronic disease but results in part from inactions that society takes—both in the public arena and in commerce and other private domains. This report argues that American society should take explicit responsibility for defining the future of disability in this country. *How it does so will reflect the country's deepest values.*"

- Disability affects or will affect everybody in the course of his or her life to a smaller or greater extent. This is particularly true as the whole world grows older and people face a considerable increase in chronic conditions and multiple co-morbidities.

- SSA is very much interested in ICF and has been awarding funds to Stanford University, which is doing work on matching ICF codes with the codes used by SSA. From 1998-2008, SSA disability insurance program applications rose from 1.2 million annually to 2.3 million annually and exceeded 3 million in 2009. These numbers are growing. Any changes that can be made to reduce the processing time for disability applications, lower the cost, or improve performance of the disability programs are important.

- There is some work ongoing at NIH that is linked to what SSA is doing. The NIH is looking into informatics and the use of ICF for capturing function. The authors Brandt, *et al.*, 2011, reviewed the gaps between contemporary models of disability and how the SSA defines and operationalizes disability. The study looked into measurements of human function using informatics using the IRT-CAT technology and item response theory in artificial intelligence software. The process starts with a question about functional status. As the person responds, the software continues to ask additional questions based on each response.

- The Department of Defense on October 12, 2011 released a request for proposals for investigator-initiated awards of $1.5 million. The application deadline is March 2012; the awards will take place in June 2012. The subject is ICF-related products in new clinical functional assessment tools. The main goal is to determine if the establishment and standardization of a common language for clinical functional assessments will improve automated disability coding and work flow within a health information system.

- There are countries that are using ICF coding, including Italy, Germany, and Japan. There are other applications used by foreign governments. Australia uses the ICF framework for its national classification of health and functioning.

- There are no studies on ICF as it applies to CFS. The literature is very limited and the focus is on fibromyalgia or chronic widespread pain from the perspective of fibromyalgia. Prodinger, *et al.*, 2011 (Germany), had 256 participants and concluded that by using ICF is it possible to construct sound clinical instruments to measure functional status and assess and monitor body functions, activities, and participation.

- Hieblinger, *et al.*, 2009, studied chronic widespread pain from the perspective of fibromyalgia patients. The study included only 33 individuals and concluded that most ICF categories could be confirmed from the patients' perspective.

- In view of the paucity of studies, validation studies for CFS are needed.

- ICF has the potential to provide valid, clinically meaningful descriptions of functional status and provide a more rational and meaningful basis for conceptualizing treatment needs, allocating resources, and assessing outcomes. ICF has the potential to encourage consideration of social, cultural, environmental and biomedical factors when developing interventions or strategies. ICF has the potential to enhance communication and encourage collaboration during the planning of a treatment. It will facilitate communication among health professionals and those involved in care planning, including families and care givers. Demonstration projects are needed among Federal payers that try to align ICF coding with various data infrastructure requirements and systems.

Section 4302 of the Affordable Care Act

- Section 4302 deals with data collection, and analysis, and reducing disparities. The first provisions that the Office of Disability had to address dealt with establishment of standards for data collection on disability status. These standards have been released and approved by the Secretary. They are a series of six questions that address functional status. That means that

every Federal survey or data set will have to incorporate these questions in a way that will facilitate evaluation and data comparison. This will take place sometime in the next year or so.

- Title XXXI is another component of Section 4302 for the Office of Disability is responsible. A small disability working group is developing survey questions under this provision in order to assess the physical accessibility of medical settings, the availability of accessible medical equipment, and the training of providers on disability awareness. So far the group has developed the questions and sent them to NCHS/CDC for review. The Secretary will then receive the disability office's recommendations and the office will decide when and how the questions will be implemented. The questions may collect information that is relevant for CFS.

Committee Discussion

Dr. Snell: I was particularly interested in this subject given that CFSAC does a lot of work in disability. ICF seems to be a system that is not illness-specific, but perhaps more importantly, does not seem to have an illness bias.

Dr. Jason: Could you give us an example of how much time takes the average person to fill out a survey? That has some bearing with our patients because they have limited energy. Are items available to be put on a website such as REDCap [Research Electronic Data Capture] so they could be used by multiple investigators? Would either SSA or your office be willing to fund a pilot study in CFS so that we could gather some basic data?

Dr. Correa-de-Araujo: It is difficult for me to tell you exactly how much time one would spend with a person because it depends on the complexity of the clinical situation and the problems that the individual may have. But if you are going to implement the ICF, you need a structure. You would have a team prepared to make the process easier. It would take more time than it takes right now to go over a situation with an individual.

As far as the availability of the information, the ICF book is online. I would be glad to send out links if needed. You should be aware that WHO and other groups continue to work to improve the system. It is my understanding that WHO is working on ICD-11. The goal for release is 2015. It may incorporate some of the sections in the ICF.

As relates to a pilot project, I would love if any of the Federal agencies do that, particularly DHHS in partnership with other Federal agencies such as SSA and the Department of Defense. Unfortunately, under current budget constraints, I do not see how it would be feasible. However, CFSAC could recommend to our Secretary that a pilot project be initiated. It would be a validation study, which needs to be done. A validation study has not yet been done internationally.

Mr. Krafchick: This is the first time I have seen the ICF structure. It is very impressive. Where would you put in current classification something like post-exertional fatigue? A question about post-exertional fatigue could be added to questions that are asked in every disability context such as, "Do you find that activity on one day forces you to curtail activity the second day?" There is nothing now that capture this information and I think that with the number of disabled people who have fibromyalgia and CFS that would be an important area to add to the data set.

Dr. Correa-de-Araujo: Absolutely, this in an important area. The refinement of ICF is an ongoing process. If a pilot study could be funded, this is an area that could be seen as a gap and a recommendation for an addition.

Mr. Krafchick: The American Medical Association (AMA) guidelines are used extensively in the United States. They are not as powerful as what you are describing. That would be the diplomatic way to say it.

Dr. Correa-de-Araujo: Exactly.

Dr. Klimas: In operationalizing ICF in a clinical setting, are there self-report forms and interviews?

Dr. Correa-de-Araujo: It is an interactive process. Perhaps the patient could self-report for certain components, but there is a need for an interactive process. When you ask questions to get a better idea of what the limitations and restrictions are, the clinician may need to be part of it. The bottom line is that it may be a little subjective, but it has always been subjective.

Dr. Klimas: Is it, in the end, a clinician's score? This sounds like it is a combination of self-reporting, such as SF 36, plus a clinician's or an assessor's perspective. In your example, the assessment of whether or not the girls could date given their impairment sounds like an interview format.

Dr. Correa-de-Araujo: It would be an interview format. You would need to have a health team trained to do so, and everybody on the team has to be able to understand the system.

Dr. Klimas: That is a problem, because most clinical sites do not have teams. They have a provider.

Dr. Correa-de-Araujo: If you do not have a team, you use the provider. But if you have a team, all have to be trained to be at the same level.

Dr. Snell: It seems to me that if it would parallel the SSA Blue Book, it would need evidence for the evaluation at some point, so there would be accepted evidence to indicate the level of disability. Is that correct?

Ms. Schaefer: What Dr. Correa-de-Araujo is talking about—the ICF in relation to CAT technology—is very cutting edge and new to the United States. What we are doing right now with the contract that we have is trying to look at a computerized version of this so that a whole evaluation team would not be needed all of the time. The process is similar to tests in which you are asked a question and if you get it right, you are asked a harder question. If you get the answer wrong, you are given an easier question to see if you can then be moved ahead. We are testing this on the internet. It is not yet developed and we do not know if we can use it by itself. It may need a team. We are looking at people's level of functioning. When I sat in on a presentation about this contract, they were looking at things like, "Can you pick up a dime off the floor? Can you use your hands in a certain way? Can you reach overhead?" Those are the kinds of questions they are asking.

Dr. Levine: I see a lot of patients on disability with CFS and I am frequently aware that the other providers who are part of this patients' network of physicians are not so up to speed in terms of filling out disability paperwork. It seems to me that you could provide a tutorial website where some of the

physicians who are not so knowledgeable about how to fill out disability paperwork could go. Where you have already applied ICF in Europe and other places, how frequently are people reevaluated? Every year or maybe every three years? Do you check in with patient to see if their status has changed?

Dr. Correa-de-Araujo: Reevaluation is part of the process. Every time the patient comes to you, you need to do another assessment. If there is a change, you need to reflect these with the codes. This is the beauty of these codes. You can clearly detect changes and be better prepared to provide additional treatments.

Dr. Klimas: If you are trying to do an early demonstration project with ICF and SSA, would you be interested in trying it in this complex CFS population? It would be a good test group to see how sensitive the measures are.

Ms. Schaefer: I think it would be very helpful. Right now we have the contract with the CAT tool and are working with that. We have been thinking about the ICF and the IOM recommendation and trying to operationalize it, but we are not far enough along for a demonstration project.

Dr. Lee: This is an excellent example of something that would have many, many uses. I can see researchers in the United States designing research around this and using it for clinical assessments. It is a framework for data collection. I did not know until yesterday that this is also in Donna Pickett's shop at NCHS/CDC. She has two responsibilities—ICD and ICF.

Dr. Correa-de-Araujo: I think it would be very useful in health outcomes research.

Mr. Krafchick: I have a master's degree in public health. The research potential of this is incredible to me. If you have the pilot program going on, could you add some questions or some areas that would begin to tease out the post-exertion fatigue aspects of these more complex diseases? To tease out how you would ask the question and get at that whole area is very important to this population as well as others.

Ms. Schaefer: I wrote down your question. I am going to bring it back and see if they have anything like that and if they do not, maybe I can suggest it.

Mr. Krafchick: I would be surprised if they did, because most people do not think of it until they have worked with CFS or fibromyalgia patients. You could add some pointed questions and you would get some powerful data.

Dr. Correa-de-Araujo: When you design the pilot you will already know that there is this gap. Those questions can be incorporated and as a result, not only will you be validating what the ICF already has, but you would be proposing new questions to be tested.

Mr. Krafchick: I was looking at your data standard for disability status and all those questions are good. It would help if there were one or two more that would begin to tease out how many of the people who are subject to the data had problems with post-exertional fatigue.

Dr. Correa-de-Araujo: As I said, this is just a set of six questions. It is just to get started. It is very expensive to add too many questions to a survey. So what we are doing right now is collecting a bank of questions generated from people sending them in and from our working group. We need to be

selective. The idea is that we will go back our bank of questions and try to incorporate them in the future.

Mr. Krafchick: You have a question asking if the person has serious difficulty walking or climbing stairs. You are going to get a lot of people with CFS or fibromyalgia saying yes. But you will not know whether they have a broken leg or are paralyzed or whether they have one of these other conditions. If you would add one or two more questions to it, you could tease that out. You are looking at populations with millions of people involved.

Dr. Jason: It seems like we are at a critical time point with this instrument. I would like to make a recommendation to the Secretary that we ask for a pilot project in this area that can be designated to one agency, potentially SSA. This is the time for us to move to the next step.

Mr. Krafchick seconded the recommendation.

Mr. Marshall: At the risk of being a naysayer, the recommendation is pretty vague. It may fall into the same trap as many of our other vague recommendations. I think we need some time to flesh it out so that the recommendation is more specific. Can we make a recommendation outside a meeting?

Dr. Lee: If you are going to vote on it, you all have to be together. We have trouble convening the entire group outside of an open meeting due to FACA rules. I would suggest that you talk more about it this afternoon.

Ms. Holderman: Is CFSAC allowed to meet by teleconference and vote?

Dr. Lee: That is not an open meeting because members of the public cannot be there.

Mr. Krafchick: In light of what Dr. Marshall said, I would offer a friendly amendment that the project be focused on ways to identify post-exertional fatigue.

Dr. Jason: Because of time issues, I will go along with Dr. Marshall. I will bring this up this afternoon.

Dr. Snell declared that the motion had been withdrawn.

Dr. Klimas: We have a serious problem just coding the diagnosis of our patients. If someone has a neurologic ICD-10 code tucked into their CFS code tucked into their sleep code tucked into a pain code, how does that work? It is possible to link things to the various codes?

Dr. Correa-de-Araujo: That is a challenge. I do not have a good answer at this point. We will need to learn together. Just to give you an idea how challenging things are, the American Geriatric Society (AGS) has a special committee that is looking into the issue of co-morbidity. The AGS will be releasing some guidance on how to manage this. When you look out there, what we have is guidance for specific chronic conditions. There is nothing addressing multiple co-morbidities.

Dr. Levine: I think you mentioned something about voice activated software. Would that be used when the patient talks about his or her limitations and then, based on the responses, the software would ask the appropriate questions?

Dr. Correa-de-Araujo: I do not have too much knowledge about it. I think that the technology will detect as the patient responds. Depending on the type of response, it can generate some questions that would go deeper into a particular issue.

Dr. Snell: This appears to touch a number of organizations within DHHS and other departments. It should be on the agenda when Dr. Lee organizes the first CFS working group.

Dr. Lee: Dr. Correa-de-Araujo is working out of the Office of the Secretary in the Office of Disability.

Dr. Correa-de-Araujo: It is a small office within the immediate Office of the Secretary. We have a policy role to coordinate efforts across agencies. We are not authorized to fund anything.

Break

Dr. Snell called a five minute break.

Centers for Disease Control and Prevention Website

Eileen Holderman, *Patient Advocate*

- Thanked Dr. Michael Miller, retired CDC official, for his responsiveness to the advocacy community and other stakeholders who were concerned about the CDC website content. He asked Ms. Holderman, Dr. Klimas, Dr. Cook, and Mr. Krafchick to review the site and submit comments on it. Each group member submitted individual comments. During that process it came to the group's attention that a medical doctor advocate named Lily Chu was conducting an independent study on the CDC website. The subcommittee incorporated her comments and submitted everything to the CDC.

- **Teleconference 1** included Ms. Holderman, Dr. Unger, Dr. Belay, and John O'Connor from the CDC. All participants were navigating the website on their separate computers. Ms. Holderman characterized the CDC officials as gracious, open-minded, and attentive to her concerns as well as those conveyed to her by advocates and other stakeholders over the years.

- **Teleconference 2**, which included Ms. Holderman and Dr. Unger, centered on the studies on the CDC website, particularly those that concern advocates—the childhood trauma and childhood adversities studies. Dr. Unger sent links that supported the premise of these studies after Ms. Holderman suggested that they are not replicated or embraced by mainstream science. Ms. Holderman has not yet examined these links.

- **Teleconference 3** also included Ms. Holderman and Dr. Unger. Ms. Holderman had looked at CDC websites for other disease groups and drew on positive examples that could be incorporated into the CFS website. These include links to other organizations. An example is the website on heart disease's link to the American Heart Association. Dr. Unger pointed out that some of Ms. Holderman's examples were links to other government organizations and noted that there are not similar organizations for CFS. Ms. Holderman suggested that this

illustrates the inequity in regard to CFS. Stakeholders would like to see on the CFS website some of the same resources, funding, and content found on other websites.

Discussion of the CDC website concentrated on three main areas: tone, language and content.

Tone – She is looking for a respectful tone that Ms. Holderman maintains is not there. She called for eliminating the current scolding, condescending tone.

Language – She is looking for strong, descriptive, medical language that is scientifically accurate.

Content – She is looking for the CDC to showcase its body of work and not focus so much on psychological studies, since CFS is a multi-system disease.

- Ms. Holderman and Dr. Unger agreed that website discussions would be an ongoing process and that Dr. Unger would look at all of the comments from the rest of the group.

- The Education/Patient Care/Quality of Life Subcommittee had the CDC website on the agenda for both of its meetings. The site affects patients' quality of life when it comes to insurance reimbursement and how the disease is portrayed. The media accesses the website and can do some damaging reports if the site is not updated and does not properly reflect what CFS is all about. Subcommittee members reviewed the website and made comments, which were forwarded to the CDC without attaching names to comments. Again, CDC staff were gracious, open-minded, positive, and accommodating.

- The subcommittee invited Drs. Unger and Belay to the subcommittee meetings and they attended. Subcommittee members appreciate the ongoing dialog that has been started. The CDC has a huge website with a lot of content. It has been hot topic, for advocates in particular.

- The two areas that have not yet been addressed are the toolkit and CME [continuing medical education]. These are probably the two most important aspects of the website. Subcommittee members did not want to rush through them. Dr. Chu is examining the toolkit.

Dane Cook, *CFSAC Member*

Thanked Ms. Holderman for being the engine behind the CDC website review.

Noted that he reviewed the website from a scientific perspective because that where he has the most expertise. He discussed three general observations:

1) The website was not wildly inaccurate and contained a lot of useful information. But I understand where the patients could find it offensive in language. I am in agreement with our subcommittee's recommendation that the website's tone could be improved dramatically.

2) The impression I got was that the information presented seemed incomplete and in many ways was cherry-picked. This was most apparent in the causes section. There were many areas of research that simply were not represented. Whether this is due to the CDC presenting its own information and not covering the rest of the field, I am not sure.

3) The information was presented inconsistently. It varied between reporting data-based fact and opinion. There were several value judgment statements—and I pointed these out in my report—that seemed to be more the bias of the CDC rather than the consensus of the scientific community. The CDC has stated several times at these meetings that their information is based on the evidence and the data. There are simply too many examples on the website where that is not the case. If this is going to be an informational website—and I think that it should be—then the information should be accurate, up-to-date, and reflect the consensus of the scientific community as much as possible. I believe that the CDC site does need to be a comprehensive site for patients, physicians, and scientists.

Dr. Nancy Klimas, *CFSAC Member*

The CME is under revision in a very proactive way. The committee reviewing the website is currently meeting once a month by conference call. Dr. Jim Jones is chairing the committee. Members include Dr. Klimas, Dr. Vincent, and Dr. Lucinda Bateman, and a number of CDC education experts and process experts. The anticipated date of completion is spring 2011. Rather than take this CME apart, it seems more reasonable to be engaged in the process of the new CME. It is well under way. Dr. Bateman is motivating all involved to push on.

Mr. Steve Krafchick, *CFSAC Member*

I was pleased to find out after our meeting that there is a link to the SSA regulations; however, the pathway is somewhat obscure. If you are going to try to help people understand what disability is about, a couple of things could be done:

1) Put disability on the home page list. It is now listed under a topic that intuitively does not make sense to an attorney, let alone a member of the public.
2) There are two types of problems that people with CFS have: post-exertional fatigue and cognitive problems. It would be useful to present the scientific data that relates to those problems along with how one would document those conditions. Most people do not know. It would be relevant to the patient community and probably pretty easy to put on the website.

Ms. Holderman: I noticed a couple of weeks ago that the CDC website has begun to change. The pages have been modified. Any movement in a positive direction is a good thing. The biggest premise for me is that I wanted the website to really reflect chronic fatigue *syndrome*, not chronic fatigue. The very first thing that one used to see on the site describes chronic fatigue. I noticed several nights ago that that has been changed. I am happy for it. I would like to see the site go a little bit further because it still makes CFS sound like depression. I would like to see more about fever and swollen lymph nodes—things that are unique to CFS, not those that could be misconstrued as overlapping illnesses such as depression, chronic fatigue, or idiopathic chronic fatigue. I want to say thank you to CDC for making the changes and thank you for opening the dialog.

Dr. Belay: The primary objectives of the CDC website when created were to raise awareness about CFS, educate the provider community about the disease, and provide basic scientific information to clinicians. I believe that we have achieved those goals to a certain extent. A lot of people visit and get information from the website. More people have become aware of CFS because of the information on the website. This has happened over time.

That is not to say that the website is perfect. By nature, websites should be reviewed and updated on an ongoing basis. Ours is not an exception. We are committed to updating the website as more data and more information become available.

The review process started as a result of the May 2011 CFSAC meeting. Dr. Klimas raised the issue that insurance companies were denying coverage for laboratory tests, citing information from the CDC website. Clearly that was not our intention for the website—to have people misuse data in a way that hurts patients. At the same time, we cannot stop people from misusing or misinterpreting information on our website. Our duty is to make the information as clear as possible. We received the comments of the CFSAC subcommittee and from Dr. Chu several weeks ago. We are still reviewing those comments. Because the information on our website was being used to deny coverage, we gave that part priority during our review and we have changed it.

We have agency rules and clearance processes that we must follow. All information that is put on our CDC website goes through a scientific clearance process within the agency. That process is ongoing. I thank the committee members, who provided comment on all parts of the website, and Dr. Chu, who provided extensive comments.

Dr. Klimas: Just to brainstorm with the committee for a moment—is there any way to undo the damage? At this moment there are policies in place with these third party providers that are quoting the CDC web page in denying tilt table tests, sleep studies, and so on. Clearly they misinterpreted the intent of the web page, but nonetheless, the policies are in play. Is there any DHHS agency that oversees third party reimbursement? How do we make them shift well-established, written policies at this point?

Mr. Krafchick: Private insurance companies are regulated by states.

Ms. Perry: I am not an expert in this area, but my understanding is that most insurance regulation is done by the states. With the Affordable Care Act, there have been some changes. I am not clear exactly what the boundaries are and what the Federal rule is, however, that is a question I can research and get back to the committee on.

Mr. Krafchick: Insurance policies are regulated state-by-state by state insurance commissioners. The only place that the Federal government has an interface is with the ERISA [Employment Retirement Income Security Act] plans, and those cover a lot of people. There could be some movement in that area. It is regulated by the Department of Labor.

Dr. Snell: I agree with Dr. Cook that there is a lot of good information on the CDC website but there is also a lot of not-so-good information and it tends to be given equal weight. You cannot always tell which should be given priority.

In part I think it is because it is a poorly designed website. Fix the things that should be fixed, but somebody should be working on a whole new website redesigned from scratch that reflects up-to-date technology and up-to-date approaches to putting together a website. Just doing it piecemeal, there are always going to be things that are problematic. It almost looks like a history of CFS. Everything that has ever been discovered or thought about the illness is still on the CDC website. We are able with inside knowledge to be able to filter things that are inappropriate, but not everybody is.

I am not sure how productive it is to include the link to St. Bartholomew's or why it was put on the website. Is it because CDC does not have its own information on those topics? It almost feels like one of those online ads that jump out at you. It certainly is not a government organization.

Dr. Levine: I want to get an idea of the timeline for making changes, especially the ones that involve patient care and reimbursement. Can we get an update from you at the next CFSAC meeting?

Dr. Belay: I think we should be able to do it within several months. Changes to the portion covering tilt tables, etc. that was used to deny reimbursements is already done. We can absolutely provide an update at the next meeting.

Dr. Jason: What is the process at the CDC for getting approval of site changes? How, as you are making the changes, can you stay in touch with the people who provided feedback? How will you make those decisions by the next CFSAC meeting?

Dr. Unger: We have already started looking at content. We were not planning an entire revision of the website. Incorporating some of the changes will require some revamping of the areas where the revised information is going. We did not intend to do something and then come back to the committee for approval on it. With the input, we think we understand the issues much more clearly. Having the conversation was really very important because there were things that I never in a million years as a physician would have taken offense at.

We have had discussions about whether we should do a focus group on this or whether we should involve a special consultant. We have to put the web page in the context of our whole program. We do not have huge resources. We are tapping into CDC's web designers. We are trying to keep a balance with our program dollars and time. We need to get a little further into this to determine how much of a revamp it will be. Once we have our content put together:

- It is submitted to the division for a review.
- It goes through the center for comments.
- It must be made 508 compliant.
- It will be put up on a test platform for review.
- It then goes live.

Dr. Cook: It would be helpful for us to get a sense of your take on our suggested changes. We do not know where you are going with it. We do not know your interpretation of the information we provided you. It would help us know if you are heading in the direction that we hoped or intended.

Dr. Unger: Our take is that we can understand the comments. While we may not make a change exactly the way the commenters suggested, we will address those issues. It is very clear where the problems are. There was a lot of concern that we are only presenting CDC research. The website is meant to present information on what CDC is doing. It was not intended to be a comprehensive research review of CFS.

Dr. Cook: Can you tell us why the government agency that studies CFS would not be a comprehensive site for CFS?

Dr. Unger: Based mission priority, we want to get information out to the clinicians and to the patients describing what is known about the illness and keep that updated. We think that PubMed and other

resources are available for researchers to find out the latest research on CFS. We have an ongoing debate at CDC about how much research to put on our network. As you pointed out, if the public goes there, it is sometimes hard to understand what is accepted versus being investigated. That is why the research part is small.

Dr. Cook: I can appreciate that thinking, but at same time, as research informs the clinic and the clinic informs research, I am not totally on board with your approach.

Dr. Lee: CDC is not the only Federal agency doing research. Dr. Unger's part of CDC is a virology division. You do not have exercise physiologists in this group. You do not have behavioral scientists.

Dr. Klimas: But you do. This is a very interdisciplinary group. When a clinician or the ER goes to the CDC website to better understand the person in front of them, there has got to be some attempt to lay out the pathogenesis and the state of the science of CFS. What primary doctor in the ER goes to NIH to try to find out how to care for the patient in front of him or her?

Dr. Unger: There are two areas on the website that deal with these issues. We do have a section on pathogenesis that does needs to be updated. That is in very broad terms. It is not detailed references. It is what the current thinking is about possibilities. Then our own research area, which was provided for information only, is the area that we are really going to shrink down so it is not highlighted, but just there as a public documentation that the program has publications.

We were also asked to consider links to other sites as appropriate in that area. We are reviewing what we can and cannot do within policy.

The whole process for this is that we have begun and hopefully by the next meeting we will have the changes already implemented.

Dr. Snell: The really positive outcome here is the lines of communication that are open. We are learning how to better communicate every time that we do it. I am not hearing anybody saying no to anything at this point. Everything is on the table for consideration. It can only lead to improvement to the CDC site and eventually, we will get it perfect.

Mr. Krafchick: The CDC cannot put its head in the sand. It has to recognize that the use of the website is going to be greater than anticipated, particularly by disability carriers and health insurance carriers. Rather than ignoring that it might be used that way, take a degree of sensitivity to that. If you do that, it will solve a lot of the problems. Also, you already have a link to PubMed. Maybe there are other sites that people should go to get that current scientific information. There are ways to keep you from having to review it and summarize it. There are so many things that can be done, and I really appreciate the openness to try to see how we can make it better for everyone.

Ms. Holderman: I mentioned to Dr. Unger that I would love to see a medical press kit on the site. Our media, unfortunately, can do quite a bit of damage. Dr. Nancy Snyderman did a report and she took everything straight off the CDC website. The result is getting that sound bite on TV that says to use the treadmill or go to a counselor. This could inflict some damage with a small sound bite.

Agency Updates

Centers for Disease Control and Prevention

Ermias Belay, MD, *Associate Director for Epidemiologic Science*, Division of High-Consequence Pathogens

Activities Since May 2011 CFSAC Meeting

Publications and Scientific Meetings

- Six CDC staff members attended the September 2011 IACFS/ME meeting in Ottawa, Canada. CDC staff gave eight oral presentations and one poster presentation and chaired two sessions.

- Two CDC staff members attended the October/November 2011 American Public Health Association (APHA) conference in Washington, DC. CDC always has a booth at the APHA conference, which attracts more public health professionals than any other conference—often more than 20,000 participants. It is an opportunity to continue educating the public health community about CFS. Educational materials were displayed and distributed at the booth. The CDC's public service announcement (PSA) was played at the APHA theatre. The PSA was created as part of the 2006 public awareness campaign created by the CFIDS Association. CDC has continued to use the PSA to raise awareness about CFS. [Dr. Belay played the PSA.] Since the 2006 awareness campaign, CDC continues to do whatever it can—as resources allow—to continue to educate different groups

- Dr. Unger gave the keynote address to the October 2011 New Jersey Chronic Fatigue Association annual conference in Eatontown, NJ.

- Five publications by CDC authors about CFS were accepted for publication.

- CDC participated in CFSAC subcommittee meetings, the CASA [collection, aggregation, storage, and analysis] working group, and the NCI SxQOL [National Cancer Institute System Management and HRQOL] working group.

Outreach and Education

- Met with advocacy groups: PANDORA (May 2011), International ME Association (July 2011), CFS/FMS [Fibromyalgia] Organization of Georgia (September 2011). Other meetings are planned.

- Hosted the COCA [Clinical Outreach and Communication Activity] call in August 2011 as part of emergency management activities. Took advantage of that call to provide a seminar on CFS. Two participants from CDC and one from Emory University gave the seminar. At the time of the call, there were 44 webinar and 33 audio lines open. The COCA course slides, webcast, audio, and transcript will be available for one year for CME credit at http://emergency.cdc.gov/coca/calls/2011/callinfo_081811.asp. As of September 18, 2011, there were 21 internet registrants and 16 CME completions.

- Printed and distributed 10,000 pieces of new health and education material to local health departments, academic centers, and CFS organizations. There is a lot of interest about CFS from state and local health departments.

- Production of new CME courses is on track for 2012. The courses cover two areas:

Clinical diagnosis and management of CFS (Team members: J. Jones, N. Klimas, L. Bateman, A. Vincent, and C. Lueckte)

CFS and sleep (Team members: R. Boneva, B. Natelson, L. Bateman, F. Togo, W. Moore)

- Just awarded a contract to a company called Center for Advanced Professional Education (CAPE). The group produces standardized patients that medical schools can use in their education process. The contract is to develop a standardized CFS patient that could be used to introduce the disease into medical school curricula.

- Secured a contract with Medscape for a CME course on CFS with a roundtable format.

Research and Additional Activities

- Established collaboration with Dr. Eric Dewart's group at the Blood Systems Research Institute for pathogen discovery using metagenomics. This group is trying to identify pathogens that may be responsible for CFS. Fifty plasma samples from acute onset CFS patients have already been sent to the institute for exploratory study.

- Made data from the Wichita Clinical Study accessible via the Research Data Center at http://www.cdc.gov/cfs/programs/wichita-data-access/index.html

- Issued three contracts for clinical assessment of CFS to try to collect clinical data to inform decision making and revisions to the CFS case definition. CDC believes that the process has to be data driven. The data will be collected from seven different clinics. The organizations are:

- Beth Israel Medical - B Natelson, PI [primary investigator]
- Neuro Immune Disorders - Nancy Klimas, PI
- Open Medical Institute – A. Koglenik, D. Peterson, C. Lapp, L. Bateman, R. Podell, PIs

Health Resources and Services Administration

Deborah Willis-Fillinger, MD, S*enior Medical Advisor*, HIV/AIDS Bureau

Overview of HRSA

- HRSA is considered a health access agency. HRSA supports direct healthcare services and infrastructure development, technical assistance, and continued learning for healthcare and healthcare access.

- Examples of HRSA support for direct healthcare services: Office of Rural Health Policy, Community Health Center Programs, Maternal and Child Health Bureau, HIV/AIDS Bureau, and health professional education support and work force development.

- Examples of HRSA technical support: quality improvement support, technical assistance and support for health information technology adoption for many of the grantees and programs that the agency supports through its funding.

- Examples of HRSA support for continued learning: knowledge management and learning communities. These are grantees that work with communities and other state and local stakeholders to improve the quality of healthcare systems, develop new strategies, and test quality measures. Some examples include the Patient Safety and Pharmacy Collaborative and the National Quality Campaign for HIV.

Latest Information from the HRSA Public Website

- A new report sponsored by the Maternal Child and Health Bureau from The National Survey of Children's Health that examines the health and well being of children in rural areas. The report links to the National Survey of Children with Special Healthcare needs. The data fields and different survey instrument tools are included.
- Currently a record 10,000 people are being supported through the National Health Service Corps.
- $3.4 million is being supplied to various states and communities for children with special healthcare needs.
- HRSA is soliciting applications for the Affordable Care Act Family-to-Family Health Information Centers. New funds are available for these centers, which assist families with children with special health needs and disabilities access services and support.

Committee Discussion

HRSA Q & A

Dr. Jason: How can people with CFS potentially profit from some of the programs? Do you have any ideas on how we can use the resources of HRSA to expedite some of the recommendations we make to the Secretary?

Dr. Willis-Fillinger: In the past I have reported on the various programs at HRSA and the fact that we do not prescribe an approach to care for patients. What we do is support organizations in communities that provide healthcare services according to guidelines. The key to allowing healthcare professionals who are supported through our programs to provide services that are aligned with those we have been talking about at this meeting is for those providers to be able to access information about care guidelines. The CME that is being developed by CDC right now is of particular interest because those are the kinds of programs that HRSA can easily mention to providers. It has always been important for us to have that kind of information. We do not direct healthcare education in terms of the kinds of education providers are required to get.

CDC Q&A

Dr. Levine: What are the topics and collaborators on the five items that you have published since May 2011?

Dr. Unger: Web-based analysis of continuing medical education courses by the Markov model, coping styles, life stress, identification of a reference gene for quantitative gene expression, and a kinase associated with interferon alpha that is induced in fatigue.

Dr. Klimas: I want to applaud the CDC for moving back into pathogenesis involving pathogens. The CDC is moving forward under Dr. Unger's leadership.

Dr. Jason: We have talked about trying to make some revisions in the current Fukuda criteria. Many of the articles that are currently being published are using the Reeves 2005 empiric criteria. Could you comment on those particular publications, those criteria, and most importantly, what the process is by which you are considering beginning to change? What is the timeframe and who will be involved in that process?

Dr. Unger: Hopefully by early next year we will have a publication that clearly explains the comparison of the standardized approach to applying the Fukuda definition [1994 definition] and the approach that we had used in the past in the Wichita studies. Everyone will find it very reassuring that the patient populations are quite comparable. I think that will relieve a lot of anxiety about what is going on. That article will also include as supplemental material a detailed explanation of how we did those criteria. That is to allay the concern about data collection in those large studies. Data analysis and testing continue for all three studies: the registry study, the GCRC clinical study, and the follow-up surveillance study.

As far as change, we are going to start with our clinical contract and getting advice from our clinical colleagues who are directly involved. We envision that that could possibly be a platform to engage people who do not actually have contracts to dialog with us and with those clinicians involved about the next steps and how we should approach this.

We are going to start with data collection. The question being asked over and over is, how do the patients differ in people's practices and is this really why we have some problems even though everybody calls it CFS and they are using a case definition? Is that why the findings in the laboratory are not always translatable? That is step number one.

Step number two is, if we have good measures of the domains (and as you know, the field is ongoing as to what are the best measures of the domains), then we try to say how can we capture this the best way. We as a field need to be a little schizophrenic and say yes, we can bring people in under a broader umbrella diagnosis, but then we cannot just group cases and controls. We have to be doing some stratification. We have to use a dynamic range in all of those measures. It is not enough to have just fatigue, but how much fatigue? It is not enough to have any one measure.

Going by what has happened at CDC in the past, we will next convene a meeting of experts. CDC does not decide any of this on its own. That is why I always say it is not CDC's definition. For good, bad, or indifferent, just like in the ACIP [Advisory Committee on Immunization Practices], CDC implements what

the committees and the recommendations are. That is how the 1994 case definition got established. 1994 is long enough ago that everyone agrees it definitely needs to be revisited.

It will be most helpful when we actually have some data to guide that discussion. Given that we are at the beginning of the contract and we are just beginning to collect the data, if all goes well, we hope that we will have the data in a one-year time frame. We can anticipate that it will be at least one year before we could start the dialog in the process.

Learning from other consensus-building organizations that I have been involved in, you have a meeting, but you need to have committees and upfront discussion and dialog before the meeting. You have things posted for comment, dialog, and discussion. Everybody needs to have a voice in what the final product is.

Dr. Jason: CDC certainly has a tremendous reputation in this country as well as internationally. Anything that you do in collaboration with others has a ripple effect throughout the whole world. There is a lot of discussion concerning the names CFS/ME, ME, and a new ME international consensus criteria published this summer. What is your thinking about the different names that are being used as well as some of these other criteria that seem to be more specific than the Fukuda criteria?

Dr. Unger: We are certainly aware of all the new definitions and the strengths and the weaknesses. I think that it has been very helpful to get this new information and to consider what other domains and what other measures should be included. I have gotten lots of communication from people saying that CFS is different from ME. I have got people that insist that it is the same thing. I think that there is disagreement. There is confusion in the field about whether it should be the same thing, whether it should be two things, whether it should be a hyphen name. Until there is clarity of what we are talking about, we cannot give good guidance. There has to be more consensuses among experts. Hopefully getting our contract started will be the beginning of the dialog. There are legitimate points to be made on both sides. I do not have the answer yet.

Social Security Administration

Michele Schaefer, *Acting Deputy Director*, Office of Medical Listings Improvement

- Clarified SSA contracts from the previous discussion of data. These contracts are not working in conjunction at this point:

CAT tool – Boston University and NIH
ICF coding– Stanford University

- Described SSA's current data as somewhat limited. The agency is developing new data and expects to have it for the CFSAC May 2012 meeting. Art Spencer, Associate Commissioner, Office of Disability Programs plans to attend that meeting. Ms. Schaefer said that the upcoming Freedom of Information Act (FOIA) request will give the SSA data specialist group more specifics about what kind of data to pull. She characterized her presentation to CFSAC as a high-level overview.

- Briefly discussed the definitions sheet on the left hand side of the blue folder distributed to CFSAC members. Title II of the Social Security Act is the disability insurance program. Title XVI, the supplemental security income program, is based on the income of the recipient. The term "concurrent" refers to a person who qualifies for both programs. The sheet also defines "disability" and "medically determinable impairment."

- Presented the first chart, Total Number of Initial Determinations for Fiscal Year (FY) 2008. The category of "All Claims" includes both Title II and Title XVI. Title XVI also includes children. The "Total" column shows the number of cases adjudicated at the initial level (2,559,342). The "Allow" column shows the number of individuals allowed (944,146). The "Allow Rate" was 36.9%. She said that a data specialist may have pull information on appeals.

- The second chart presented the number of individuals who are receiving disability benefits based on CFS as of May 2009. The chart shows data for people with CFS as their primary impairment (1,034) and their secondary impairment (999). The impairment status is determined at the time of adjudication. The chart breaks down recipients according to those under Title II (subcategories: worker, widow, disabled adult child) and Title XVI (subcategories: adult, children).

- Presented three charts tracking denial counts for FY 2008— one for multiple sclerosis and two for CFS. The first CFS chart tracked denials at the initial adjudicative level (2,877 total) and the second CFS chart tracked denials at the second (reconsideration) adjudicative level (679 total).

- CFS determinations as a primary impairment are less than one tenth of one percent of SSA's total determinations. An SSA data specialist determined that the number is too small for a statistical analysis.

Dr. Lee: A data specialist could combine data from two or three years and you would get better numbers. We have just recently found out about the SSA data. Ms. Schaefer came in to pinch hit at the last minute. She has done a yeoman's job. We have a commitment from Ms. Williams to work out the best way to get more data. There seem to be some hurdles to overcome. That is one of our goals for the spring CFSAC meeting.

Dr. Klimas discussed several issues with the SSA data. She noted that 2,877 CFS patients were denied coverage at the initial adjudication level and 679 were denied at reconsideration. She asked how many people were approved at the reconsideration level. That number is important, she said, because CFS patients who get an initial denial frequently do not have the courage to go back for an appeal.

Dr. Klimas: One of our subcommittee issues with SSA has been the sense among patients that there is a regional bias in the appeals process and locations where people are more likely to win an appeal. Patients have said that there are areas where you dare not try because it is not going to happen. That would be helpful for you to know in the adjudication training process. If you could present data looking at regional variation, that would be very helpful.

But this information is great. It is the first time that we have ever gotten data back after a request to SSA. It is hugely helpful to have numbers. It is hard to talk in generalities. I think we will be asking more questions, but they will be more precise because now we know what kind of data you can provide.

Dr. Levine: This may be a question to be answered at the next meeting. Is there a significant difference in the awarding of disability over the years? Is there an incremental increase in the number of claims allowed over the last five years? What may have caused that? Is it due to a change in adjudicators or their learning curve, particularly as it concerns CFS?

Ms. Schaefer: I wonder if the ruling that we issued on CFS made a difference? That would be interesting to see.

Dr. Jason: I want to thank you for coming in with numbers. There have been years and years where we asked for these basic data and it is now coming in. The incidence numbers seem a little low. I think we need to think about whether people are being misclassified into some other condition for which it may be easier to get disability. There may be a way of teasing that apart with information or research that your agency does. It might be good to compare that work with community prevalence data on both incidence and potentially even prevalence and see the mismatches so we can better understand the nature of the problem.

Ms. Schaefer: When the primary and secondary impairment are recorded, the person may have CFS but not have it recorded as the primary or secondary impairment. That is a limitation of the data.

Dr. Snell: We may want to think about reviving the idea of listing alternative diagnoses that people could potentially get in lieu of CFS and include those in our data comparisons.

Mr. Krafchick: The key regulation is 99-2p, which if I understand it correctly, is a 1999 regulation. I was struck by the 36.9% that are allowed out of the two million claims. It would be interesting to know that kind of information for CFS. Often SSA attorneys will go for a mental health classification rather than fight for CFS. That may account for some of the poor data on CFS. It is not a mental health condition, and that is part of the problem with the whole system. It would also be helpful to see what happened with the CFS population in appeals. A lot of people get denied. The general sense is "I am going to get denied at the initial and reconsideration level, but when I get an attorney and fight it, I am going to get my benefits." That is what I hear from the SSA attorneys that I refer people to.

Ms. Holderman: How will you handle answering my extensive list of pre-meeting requests for SSA?

Ms. Schaefer: We could go through the list and see. I think there are some that have been answered previously.

Ms. Holderman: I looked at information requests from the previous patient advocate member of CFSAC going back to 2005. The answers did not meet her expectations. It was not up to the quality of the data that you submitted. Data has changed and your system is much more technologically savvy now.

Ms. Schaefer: Is it a data question or a policy question?

Ms. Holderman: Both.

Dr. Lee: Those questions were given to Cheryl Williams, the *ex officio*. I do not know if Ms. Schaefer was given those questions. We did not know that Ms. Williams would not be able to be here until Wednesday or Thursday. These tables were originally provided to us by Ms. Williams. We were working with her. With the last minute change, we did not get Ms. Holderman's questions addressed.

Dr. Snell: The data that we got from our previous round of questions did not appear to answer the questions that we thought we asked. It is worth trying again. The *ex officios* are on the subcommittees and if they can take part in the phone conversations that occur in between meetings, a lot of the work can be done in terms of discussing what questions can be answered and how best to ask them.

Mr. Krafchick: Do you know where the data for CFS comes from? Is it only from the cases that went to an ALJ [administrative law judge] decision or are they reconsideration? Where do you get the primary and secondary bases?

Ms. Schaefer: At any level, the adjudicator records primary and secondary impairment codes. I did not bring any ALJ data. That would be the third level of appeal.

Mr. Krafchick: Then it is very clear that the prevalence data is way off.

National Institutes of Health

Janine Austin Clayton, MD, *Deputy Director*, Office of Research on Women's Health

Addressed the ongoing changes at NIH:

- Noted that Dr. Vivian Pinn, former Director of the Office of Research on Women's Health (ORWH), through which the Trans-NIH ME/CFS Research Working Group is managed, retired eight weeks ago. Dr. Clayton is now acting director.
- Conveyed greetings from Dr. Dennis Mangan, former Chief of the Infectious Diseases Branch, who retired less than eight weeks ago.
- Assured CFSAC that as acting director of ORWH, she and the office remain committed to continue the momentum that has been developed over the last two years to advance research on ME/CFS.
- Dr. Charles Wells, a senior advisor in ORWH, has agreed to be the NIH *ex officio* member to CFSAC. Dr. Wells will also be the point person for CFS in ORWH. He has been at NIH for 26 years and in ORWH for almost six years.
- Noted that one of the concepts that she is working on in the ORWH is working teams and redundancy.
- Pointed out Dr. Candace Tingen in the audience. Dr. Tingen is a fellow with the American Association for the Advancement of Science who works in the ORWH. She is going to bring her strong communication skills and her research background to help move things forward.
- CFS will be part of the ORWH research working team.

Charles Wells, PhD, *Senior Advisor*, Office of Research on Women's Health

Dr. Wells presented a briefing on NIH activities since the last CFSAC meeting:

- DHHS/NIH Blood XMRV Study was unable to identify the virus in blood samples.
- There is an NIH clinical study looking for other retroviruses in a large cohort of CFS patients.

- NIH has organized a Special Emphasis Panel (SEP) in the Center for Scientific Review to review all of the ME/CFS applications. Dr. Cheryl Kitt will discuss the SEP.
- NIH funded 20 grants during FY 2011 that are relevant to ME/CFS. Dr. Wells presented a list of eight examples. They include co-morbid chronic pain conditions (National Institute of Dental and Craniofacial Research), development of small animal models of CFS (National Institute of Allergy and Infectious Diseases), stress effects on viral reactivation (NIAIDS), comprehensive molecular profiling of CFS (National Institute of Arthritis and Musculoskeletal and Skin Diseases), neuropathic abnormalities (National Institute of Neurological Disorders and Stroke), and brain mast cells and CFS (NINDS). Dr. Wells noted that progress reports on the 20 grants may be available by CFSAC's May 2011 meeting.

Trans-NIH ME/CFS Research Working Group

- ORWH coordinates the activities of the Trans-NIH ME/CFS Research Working Group. It is composed of representatives from 17 of the 28 NIH Institutes and Centers. The group has monthly meetings. Outreach includes a website and email listserv.

- The working group organized the April 2011 State of the Knowledge (SOK) Workshop on ME/CFS, which drew 32 investigators with expertise in basic, clinical, and translational sciences. Dr. Wells did not know if the workshop included any experts on reverse translational science. The workshop was watched by nearly 900 viewers via NIH VideoCast and 100 in-person attendees.

- The group sponsored a Grant-Writing Workshop at the September 2011 IACFS/ME meeting in Ottawa, Canada.

- NIH is preparing to reissue ME/CFS Program Announcements. The mechanisms of support would be R01 and R21.

SOK Workshop

- Purpose: To bring together patients, advocates, and scientists to review and discuss the opportunities and gaps in ME/CFS.
- The workshop report went online in mid-August 2011 and has been downloaded nearly 4,000 times.
  Download address: http://www.orwh.od.nih.gov/CSF%202011/ORWH_SKW_Report.pdf
  Hard copies are available by calling Dr. Wells at (301) 402-0361.
- ME/CFS research gaps identified at the workshop include weak study designs, unknown etiology, lack of validated biomarkers, lack of case definition and diagnosis, more genetic studies needed, more experts needed in the new discipline of synthetic biology, more of a system biology approach needed, symptomatic treatment, and paucity of investigators.

Sheryl Kitt, *Deputy Director*, Center for Scientific Review

- The Center for Scientific Review (CSR) funds nothing, but does review grant applications. CSR receives all grant applications that come to NIH. CSR is also the home for the Congressionally mandated Special Emphasis Panel (SEP) for CFS. The Congressional mandate for this study

section has been in effect for more than a decade. Even though CSR does not make any funding decisions, the institutes do. Many CFSAC members have served on the SEP and applied for grants.

- The problem is that the SEP receives very few applications for CFS research. Over the last two years, CSR has received between six and 18 applications per study section. A real effort has to be made to get investigators interested in CFS. The NIH cannot fund applications that it does not see. The funding success rate is high because there are not that many applications. In order to be successful in improving the health of individuals with CFS, people need to do research and be encouraged to apply for research support.
- The SEP changes expertise every few months. This panel meets three times a year. CSR tries to bring back some of the same reviewers, but that is dependent on the applications. It is hard to have a standing committee with set expertise when the applications change every few months.
- If an applicant is not studying just CFS, and requests that the applications be reviewed in other study sections based on the science, the applications will likely be reviewed where requested. Applicants may not do better if they go outside the CFS study section. The success rate is quite high in the CFS study section because the number of applications is low. It may give a false impression about relative success. The bottom line, whether applicants are being reviewed in the CFS SEP or in any other study sections, is that the number of applications is small.
- A standing committee usually reviews about 60-100 applications in a study section. CSR has 240 standing study sections and about 1,000 SEPs. The current number of CFS applications would not support a standing committee.

Dr. Klimas: Is the number of CFS applications an increasing or static number?

Dr. Kitt: It is pretty static. There have been changes in peer review over the last two years. The applications got smaller, the criteria are somewhat the same, but they are all scored. The priority scores that applicants receive are based on whether the research will make a difference in clinical practice, patient care, and the scientific field. The burden is on the applicant to write it that way. The relative number of applications has not changed because of that. Another trend has developed in the past two years: if an individual is funded the first time, the person tends to not come back a second time. The CFS SEP is not getting competitive renewals very often.

Dr. Klimas: I think that some of the things that could encourage additional investigators could come from NIH. One would be training grants. We also do not have an easy way to come in with clinical trial applications, and that is where we are in our field. We have a big problem there. Also, using an interagency coordinating committee to try to patch together the funding has dramatically limited access to program projects and center grants. That must be tackled head on. It has been a recurrent theme. We have mentioned it many, many, many times.

I know that when NIH has tried to jumpstart fields in the past—say, the field of geriatrics—the Center on Aging went from a "sketch" area of doing science to one of the most predominant and well-respected areas of doing science. This was mainly because NIH made a full-court press effort to draw in people from other fields, encourage K awards, encourage training grants, and encourage centers and programs. That is the way to jumpstart a field—to get that kind of collaborative, total program idea behind the funding structure.

Dr. Kitt: I think those are great ideas. With regard to centers, I know that the ORWH had supported centers. The specialized centers for research had components on CFS and temporomandibular disorders, but the fellows tend not to continue on with their independent research.

You mentioned collaboration. There is no reason not to put collaborative multi-investigator applications together. There is nothing preventing that, with some training slots on your RO1s. By the way, most fellows get trained on RO1s and not training grants, including myself. But that does not mean that an institution should not submit one. You can contact program staff in the neurology institute, the arthritis institute, wherever you wish, and discuss with them what your training program may look like.

The other thing is fellowships. F32s are for post-doctoral individuals. We have not seen any over the last two years. If you have fellows in your labs, please encourage them. The fellowships and the career awards with a K have a much higher success rate than RO1s or R21s. This practice is still in effect throughout NIH: there is a different pay line that is beneficial to new investigators who never had NIH support within 10 years of their terminal degrees. The differential in the pay line is twice as good. For these people, RO1 is the way to go. It provides five years of support and institutes are looking for them. Institutes have a mandate to try to fund as many early stage investigators as possible.

In the last two years, there were no new investigators in CFS that were reviewed. That is a problem for the field—that new investigators are not even submitting applications.

Dr. Jason: [Question for Dr. Wells] Dr. Mangan is a person who generated good will among the scientific and patient community, as did Dr. Eleanor Hanna. There has been a sequence of people with whom CFSAC members have developed trust and knowledge. In light of the changes, how do we figure out a way of getting more stability so that the year and a half or two that it takes one to learn the connections, people, and field can profit CFSAC in a better way so that we can work collaboratively?

[Question for Dr. Kitt] Your message to us repeatedly is how do we get more applications? What I hear from investigators is that because it is an SEP, sometimes the membership changes so that the reviewers are different on the panel when the revisions come in. These reviewers sometimes have new sets of issues. I recognize that you cannot have a standing committee without more applications, but how do we deal with this issue of a different panel reviewing revised applications?

Dr. Clayton: As a clinician, I was profoundly touched by the public testimony. We included CFS in all five of our strategic planning meetings. I am specifically committed to continuing the momentum. Continuity is an issue. I am hopeful that because Dr. Mangan was reporting to me all along in the last few years that I can provide some of that continuity. I think that my strategy to organize the office around working teams and develop some redundancy will help with continuity as well. I hope that you will be willing to look at this in a new way. After 20 years with the same leader, this is a new time. I am encouraged hearing all the interest around the table. As a formal clinical investigator, I recognize these issues. We have to work together and we have to find creative ways to accomplish things in this fiscally constrained environment. There are creative ways to capitalize on existing investments.

Dr. Kitt: As far as continuity of reviewers, this is not unique to this SEP. It is true of every study section. We do not guarantee continuity of reviewers. Since the number of applications is small and the number of reviewers is small, there is always the possibility of disclosing a reviewer's identity, which we can never do. We try to have at least one person return and more if needed. It is based on the expertise. The applications are different every time so we need new people to come in.

Mr. Krafchick: Maybe the next step would be to do a State of Treatment meeting so that all the people who are treating CFS can come up with some shared knowledge in that area.

Dr. Klimas: Are intramural and extramural both in the trans-NIH working group? What I am worried about is clinical trials. There is no avenue to get them done. If we could work with the intramural clinical trials group at NIH to try to get some of this early work done it could be very helpful.

Dr. Clayton: The Trans-NIH ME/CFS Working Group has membership from 17 institutes and centers, not specifically the intramural program. As you know, funding through intramural and extramural are distinctly different. Intramural represents about 10 percent of the entire NIH budget. There are specific ways that intramural can collaborate. One of those is called a bench to beside award that allows intramural investigators to collaborate with extramural investigators. I would recommend this specific mechanism. I can put you in touch with the folks who oversee that program to identify the next dates and see if we can match you up with somebody in intramural to be able to pursue that.

I recognize your frustration regarding clinical trials. These are issues that I will take back to the working group and ask for their recommendations. In order to move things forward, we really do need to work together, including the ICs [institutes and centers].

Dr. Klimas: Can our program announcement include clinical trials?

Dr. Clayton: The working group is reviewing that now.

Lunch

Dr. Snell declared a recess for lunch.

Public Comment

Dr. Lee thanked all public commenters as well as members of the public attending the meeting in person and via live audio feed. She highlighted the importance of public comments to each CFSAC meeting.

Dr. Barbara Cottone (by phone)

- Anesthesiologist fully disabled with CFS for 15 years.
- The most damaging mischaracterization of the syndrome is not that it has a psychiatric basis, but that its symptoms are based on a compromised immune system leading to a chronic infectious disease. CFS is not a chronic infectious disease. It may be triggered by an infectious agent or an exposure to some toxin. Whatever the initial insult, the end result is a neurologic deficit resulting in an autonomic nervous system that does not respond properly to activity.
- As to immune abnormalities, this is not an immunodeficiency as in AIDS, leukemia, or immunosuppression by chemotherapy. The acronym CFIDS is thus a misnomer. She has thought the immune findings in CFS to be epiphenomena and asked a respected researcher about this. The response: A few studies might have been done, but it is unlikely more data

would do anything. After attending the IACFS meeting, her sense is that many of the people there are not really interested in data anymore. The whole CFS immune thing has become religion, as demonstrated by how the XMRV story has played out.

- Research done on a broad spectrum of pathogens has found no one single agent underlying this illness. Congress gave the CDC $20 million in the 1990's to define and limit any possible public health threat or potential epidemic and the CDC found neither. The XMRV fiasco has not only wasted time and resources, it has made a travesty out of scientific investigation into the disease and raised and dashed the hopes of those who suffer with CFS.
- A recent $10 million philanthropic effort launched in Oslo will involve virologists, epidemiologists, and neuropsychiatrists and will revisit the same realm explored for the last 30 years. Time as well as money will be wasted in another infectious disease probe.
- It is worth noting that people so badly afflicted with CFS that they cannot crawl from bed to bath do not transmit the illness to family, caretakers, or partners via air, water, or body fluids. Therefore, an alternate paradigm is necessary for progress.
- Future research might be inspired by past papers published by the late Dr. David Streeten in the 1990's characterizing CFS as a "form of delayed orthostatic intolerance" and demonstrating constricted blood flow volume in CFS patients. Other relevant research:
- Work by Dr. Julia Newton on the relationship between exercise-related autonomic functioning and a decrease in pH in striated and cardiac muscle.
- A study at Georgetown University by James Baraniuk delineating cohorts of abnormal proteins in the cerebrospinal fluid of CFS patients.
- The deletion of the term ME from ICD coding and the supplanting of it with CFS would have devastating consequences. Keeping the term myalgic encephalitis in the forefront is key. CFS should be classified separately or subordinately.
- Paramount to the future of understanding and treatment of CFS is emphasizing the primacy of a neurologic basis of the disease. This will give those doing the most promising research a chance to gain some desperately needed traction and be funded as they should.

Denise Lopez-Majano (by phone)

- Phoning in testimony because her sons are too disabled with ME/CFS to attend more than one day of the CFSAC meeting and they attended the previous day.
- Thanked Drs. Snell, Klimas, and Jason for their service on CFSAC.

- Noted that the goal for her testimony is to get things done:

1) Supported use of the International Consensus Criteria for ME published in October 2011. Although it is a working case definition, using it will put everyone on the same page, using the same definition to identify the same patients. Doing so is critical to funding, research, and education. Asked all CFSAC members who agree to raise their hand. [No CFSAC members raised their hand.]
2) Require that CDC, NIH, and all of DHHS submit all materials related to CFS to CFSAC for review. A case in point is the AHRQ national guidelines from 2006 on the management of CFS, which list CBT [cognitive behavioral therapy] and GET [graded exercise therapy] under interventions and practices.
3) Avail CFSAC of the expertise of advocates in an ongoing manner. Examples:
   - CFSAC recommended in May 2011 a DHHS workshop to create a more efficient and fair

disability assessment process to benefit patients and adjudicators alike. Patients have implemented a survey about Social Security disability and income that will provide useful information for this workshop. Advocates can also assist with extensive knowledge about young people with ME/CFS.

- Partner with advocates to consolidate CFSAC recommendations.
- Partner with advocates to help prepare CFSAC presentations at the 2010 Education Department conference on the impact of ME/CFS on academic careers.
- Involve the ME/CFS community in amending the CFSAC charter, including the inadequate bylaw stipulating real-time video streaming of CFSAC meetings and workshops and an addition
- Allowing for the staggering of the expiration date of committee member terms. The terms of
- Seven of the 11 CFSAC members expire in 2014, setting a daunting learning curve.
- $18 million in ME/CFS research funding over the last 10 years has gone astray. This cannot be
- Allowed to continue.

Ms. Lopez-Majano ended by emphasizing the importance of real-time video streaming for community participation.

Charlotte von Salis

- Had planned to attend the CFSAC meeting but is too sick to do more than move around her home when needed.
- Directed her testimony at Drs. Wells and Kitt.
- Along with Pat Fero, meticulously investigated questionable grants awarded by the NIH budget office for CFS research from 2000 through 2010. Their work reveals that some $18.5 million was spent on non-CFS studies. This is appalling.
- It is also appalling that NIH lied to patients, researchers, and the public at large by representing that these grants are CFS expenditures. Considering the paltry funding that CFS receives ($6 million in 2010), it is especially insulting.
- The $18.5 million does not even include questionable grants—often renewed for years—that resulted in little of substance for CFS. One example: the use of Viagra to improve blood flow to the brain. After five years and close to $180,000 in funding, the researcher has not completed enrollment of the 30 people he wants to study.
- Why is this happening? Look at the funding opportunities for CFS on the Trans-NIH ME/CFS Research Working Group web page. The two—an RO1 and an R20—that are specific to CFS really are not. The NIH institutes and centers that might fund such grants are looking for applications that study CFS as a co-morbid condition, encouraging researchers to throw in the words “chronic fatigue syndrome” to win funding for their non-CFS interests. The implication is that CFS is not worthy of research by itself.
- Numerous studies on the pathogenesis and potential etiology of CFS can be built upon. Continuing to study symptoms is a waste of time.
- What is sorely needed is more targeted funding. Dr. Kitt has urged the encouragement of new researchers to submit grant applications. The lower application rate is likely due to the perception that NIH does not care about ME/CFS research. Ms. von Salis asked Dr. Wells to tell Dr. Collins to give back the misspent funding in the form of a request for applications

- NIH spends $3 billion on HIV/AIDS, which is now a manageable chronic disease with a prevalence rate similar to ME/CFS in the United States. Multiple sclerosis received $133 million in NIH research funding in FY 2010 and Lyme disease, $24 million. Where is the funding for ME/CFS?

Joseph Landson

Mr. Landson gave his testimony dressed as his alter ego, Dr. Neal Ander Thal, public affairs director for the "Cave Doctors of America," an affiliate of "International Cave Doctors," the oldest medical association on the planet. "Dr. Thal" made the following points:

- For decades, ME/CFS has been locked in a false dichotomy between a psychogenic model and an infectious model—paradigm may be a better word than model. While there is some psychiatric manifestation, psychogenesis fails to explain many neuron-endocrine symptoms. Meanwhile, the infectious model remains unproven. Perhaps we need to look more broadly to other transmissible agents such as the prion—the conformational protein.
- By blanking the prion gene—or deleting the GPI [glycophosphatidylinositol] prion anchor—researchers have created prion infections that cause none of the neuron damage we would otherwise expect. These synthetic prion infections have generated amyloid plaques, including, in one case, cardiac amyloidosis. This stiffens the walls of the heart and is one of the potential etiologies for orthostatic intolerance.
- Known prion diseases manifest in the form of sleep disturbance, emotional lability, and cognitive dysfunction.
- In the recent Rituximab study in Norway, killing off and regenerating B-cells—the lymph-node-produced memory cells of the immune system—reduced or eliminated ME/CFS symptoms in two-thirds of subjects. No one is sure why. Prions target the lymphatic system and can infect it without prion protein expression in the B cell. It is not known how prions convey information beyond their shape. Could they be exploiting information from the patients' own immune systems? Medicine needs to look at all the transmissible etiologies, not just the usual suspects.

Dr. Joan Grobstein

Dr. Grobstein, a physician, commented on CFSAC procedural issues:

- It is imperative that live web-based videocasts of CFSAC meetings continue. Patients are not able to hold a phone for several hours, often cannot concentrate on a pure audio feed, and cannot see the slides. Failing to videocast violates the CFSAC charter which states, "To the extent possible, meetings are broadcast over the internet as real-time streaming video." Audio broadcasting is not an adequate accommodation.
- The procedures for public testimony must be transparent and consistent. The *Federal Register* CFSAC meeting notice stated that time slots would be given on a first-come first-served" basis, then priority was given to people who have not testified before. Many

Dr. Grobstein said that the following recommendations are critically needed now:

- The NIH should issue an RFA for projects to elucidate the role of B cells in ME. An additional RFA should be issued for projects studying the mechanisms involved in post-exertional malaise, orthostasis, and oxidative stress in ME, including possible viral or retroviral associations and potential therapeutic options. Money that was misallocated to research that was not related to ME should be traced and redirected to promising ME research.
- The gross inaccuracies on the CDC website, which cause harm to patients, must be revised within 30-60 days.
- CFSAC must reject further use of the inexact Fukuda criteria and endorse the Revised Canadian Consensus Definition (2010). The CDC must stop all research using the empiric definition as of tomorrow and immediately begin epidemiologic and longitudinal studies of cohorts defined by the Revised Canadian ME/CFS Case Definition (2010), with special emphasis on cases that occur in geographic or family clusters.
- A collaborative project between the CDC, HRSA, and AHRQ must be funded to identify and care for the sickest, housebound, and bed bound patients who are often not receiving any medical care at all. This is a national disgrace. Programs to deliver care should be in place within one year.
- The ICD-10 coding issue should be resolved in a way that prioritizes the needs of patients above the needs of researchers and statisticians. If researchers wanted their results preserved for posterity, they should have insisted on a more appropriate name and definition in the first place.

Substantial progress on these five recommendations should be made by the May 2010 CFSAC meeting.

Mike Munoz (testimony read by Marly Silverman)

- Executive director of the Rocky Mountain CFS, ME, and Fibromyolgia Association and on the steering committee for the coalition 4 ME/CFS. The coalition made the proposal to the NCHS/CDC to have CFS restored to G93.3 as it is in the WHO's ICD-10.
- CFS is already classified in the index area of the WHO ICD-10 under G93.3. The coalition and CFSAC (as recommended in 2004, 2005, and this year) are not asking for something new or different. We want to get the United States in line with the rest of the world.
- Having CFS listed under "chronic fatigue unspecified" erroneously indicates that little is known about the disease. Having CFS coded the same as ME, as the rest of the world does, indicates that CFS is a neurological disease with muscular pain and inflammation in the brain or spinal cord. Studies show that this is the case with CFS cohorts.
- We must distinguish and eliminate from our cohorts those who have "chronic fatigue unspecified."
- The premise the NCHS/CDC gave for separating CFS from ME and PVFS [post-viral fatigue syndrome] is that CFS does not have a viral trigger. Research has shown that this is incorrect. Even the CDC acknowledges that the majority of CFS cases have a viral trigger.
- The term "CFS" will not become obsolete as long as it has its own diagnostic code. If CFS and its criteria are to disappear, CFS must be put in the code with ME.

- The coalition strongly discourages NCHS/CDC Option 2 because it makes ME and PVFS get a new label of "other chronic fatigue syndromes."
- The coalition's Option 1 is in line with NIH, which now refers to the disease as ME/CFS; with the very popular Canadian Consensus Criteria; and with the new International Consensus Criteria.

Marly Silverman

- Founder of PANDORA, which has the mission of restoring quality of life to individuals with neuroendocrine immune diseases. Also has suffered with ME/CFS and fibromyalgia since 1998.
- On May 26, 2011, PANDORA met with representatives of the CDC CFS Research Program, including Dr. Beth Unger, her team, and contractor Danna Brimmer. The meeting was the result of a letter sent by PANDORA to welcome Dr. Unger to her new position.
- Two recommendations in the welcome letter have been put in place. One is the ongoing communication with patient advocacy organizations and the other is the granting of contracts to physician/researchers in the ME/CFS field.
- PANDORA was pleased to hear Dr. Unger using the term CFS/ME during her presentation at the 2011 IACFS/ME conference in Ottawa. PANDORA also acknowledges that Dr. Unger has publicly clarified that the CDC's CFS program uses the 1994 Fukuda definition instead of the 2003 Reeves empirical definition.

During the meeting with Dr. Unger, PANDORA reiterated its major concerns:

- The revision of the overall scientific material on the CDC CFS website, which should have a bibliography representative of the whole literature, not simply what the CDC researches.
- The revision of the Physician Training Tool Kit
- The downsizing of the number of social and behavioral studies, since CDC CFS research is housed in the Division of High-Consequence Pathogens and Pathology.
- CFS is both viral and non-viral.
- CFS should be classified in the neurological chapter in the ICD-10-CM.

Ms. Silverman provided the following recommendations to CFSAC concerning the reclassification of CFS in ICD-10-CM:

- Reiterate that CFS is a multi-system disease and reject any proposals to classify CFS as a psychiatric condition.
- Continue to reject the current classification of CFS in Chapter 18 of ICD-10-CM under R53.82.
- Continue to recommend that CFS be classified in ICD-10-CM under "diseases of the nervous system" at G93.3.
- Recommend that CFS remain in the same code or sub-code as ME because CFS includes both viral and non-viral triggers.
- Recommend that an "excludes 1" be added to G93.3 for chronic fatigue.
- Recommend that these changes be made before the roll out of ICD-10-CM in 2013.

Ms. Silverman emphasized that the reclassification of CFS in ICD-10-CM is not a patient advocacy initiative, but a long overdue scientific process that has been documented by CFSAC in its recommendations in 2004, 2005, and May 2011. PANDORA believes that because of the lack of resources and gargantuan challenges within the CFS scientific community, the reclassification was not initiated directly by the international scientific organization that represents the field. Ms. Silverman is a member of IACFS/ME and is engaging the organization in this process.

Ms. Silverman closed by proposing two CFSAC recommendations:

- Establish a new strategic plan without necessarily waiting for a new charter.
- Look to the DHHS autism advisory committee as a model, with its panels for patient and public communications, tracking of committee progress, and an annual report to Congress.

Matina Nicholson

- Has had ME for six years. Thinks that CFIDS is a degrading term that contributes to the lack of respect and funding that patients deserve from the medical and research communities.
- Lost her career in pharmaceutical marketing and research. Is now supported by Social Security disability. It does not cover her medical costs, so her parents, who are in their late 70s, must support her. When they leave, she does not know who is going to take care of her.
- Wants her life back, and the only way to do that is to stand up and fight in a positive, productive manner. All those involved in the field need to all come together and find a solution.
- CFSAC repeatedly asks for centers of excellence and NIH and the CDC repeatedly undermine them. Children are losing their childhoods and patients are dying from suicide and complications from medications.
- Funding for CFS must be evaluated. NIH supports underage drinking prevention with $155 million. CFS gets $6 million. This is complex disease and a life-long struggle.
- Public service announcements need to be more national, similar to the anti-smoking and HIV awareness efforts.
- The disease name must be changed to reflect the seriousness of the disease. We do not call chicken pox the itch disease or insomnia the awake syndrome.
- Thanked Dr. Levine for her care above and beyond the call of duty.

Dr. Lee noted that CFSAC made the decision in the *Federal Register* to give priority to people who have not spoken before. All people who requested to speak and provided written testimony—a requirement in the regulations that govern CFSAC—were able to speak. All CFSAC staff who worked on testimony was new to the process. There were admittedly some bumps in road. Dr. Lee said that she and her staff will do better the next time. Dr. Lee said that she is personally committed to having as many people speak as possible.

Dr. Snell suspended the afternoon break in order to accommodate **Dr. Jason's** presentation, which was rescheduled from the morning portion of the meeting. Dr. Jason took the lead on the project, which required organizing a large group of academics, a task that is not insignificant on its own. Dr. Snell commended Dr. Jason for everything he has done on the project.

Minimal Data Elements for Research Reports on CFS

Dr. Leonard Jason, PhD

- Dr. Jason noted the list of participants in the project, including Drs. Unger, Dimitrakoff, Houghton, Cook, Marshall, Klimas, and Snell.
- The problem the group confronted is the variability in CFS research highlighted at NIH's 2011 State of the Knowledge CFS meeting. This, prompted researchers to consider the critical information that should be included in published CFS research reports.
- The CFS research community is dealing with difficulties comparing data collected in different laboratories regarding descriptions of items such as sampling methods, patient characteristics, and clinical assessments.
- Currently there is limited clinical and laboratory information presented in CFS scientific articles that are published. Available checklists for describing phenotypes have considerable overlap and they contain arbitrary variations in wording and structuring and are applied inconsistently. There is a need for improved standardization of procedures and increased communication across research groups.
- Since June 2011, the group has been working toward developing a consensus on the minimum data elements that should be included in all CFS research reports that are published. These recommendations are intended to improve the consistency of reported methods and the interpretability of results.
- Adherence to minimum standards and increased reporting consistency will allow for better comparisons among published CFS articles, provide guidance for future research, and foster the generation of knowledge that can directly benefit patients.
- The need for minimum reporting is not new to the field. Biological and biomedical communities are developing minimum reporting guidelines for publication of scientific articles. For example, Minimum Information for Biological and Biomedical Investigations (MIBBI) is a compilation of "minimum information checklists" that outline the key information needed for reporting results of experimental studies using specific techniques. Examples: fMRI studies or studies using cellular assays (Taylor *et al.*, 2008).

Framework

- The group's work will provide a framework for improving the consistency of what is reported in CFS research articles and will hopefully ensure that appropriate scientific standards are met.
- The group will suggest validated instruments and procedures that could help build consensus with respect to research methods reported in journals.

Essential Elements 1

The group believes that there are certain essential elements and recommends that as many of the following tests/criteria as possible be included in order to better define and standardize patient populations between studies.

Case Definitions

There has been ongoing discussion of the number of case definitions, including the Fukuda criteria, MEICC, Canadian Criteria, and the empiric criteria. Researchers need to at least report which definition is being used. More importantly, there is going to ultimately be a need for scientists across the world to focus on one set of standards and use those standards in research. That is the only way to get both the credibility and the consistency across samples. That is the next task that needs to be worked on.

Study Design

Types of study include case-control, case-only, cross-sectional, and longitudinal. They must include:

- Randomization protocols when employed
- Primary and secondary outcomes specified
- Site and method of recruitment
- Time frames (for example, specific dates and time intervals when data were collected)
- Language(s) used to collect data
- Statistical methods for primary and secondary analyses

Exclusionary Medical Conditions

- List the medical conditions that are considered exclusionary.
- List the medical conditions considered co-morbid and not exclusionary.
- Describe the method of identifying medical conditions.
- Note the laboratory tests and cut-off values for exclusion.

Demographic Characteristics

All articles should include:

Age, race, ethnicity	Employment status
Education	Insurance status
Socioeconomic status (SES)	Disability status
Body mass index (BMI)	Mode of onset
Marital status and children	Duration of illness
Living arrangements	Exacerbating factors and triggers

Self-Reported Functional Impairment and Physical Activity

A number of things could be used:

- Medical Outcomes Survey Short Form-36, Short Form-12, Sickness Impact Profile (SIP)
- Validated instruments for the assessment of physical activity behaviors such as the International Physical Activity Questionnaire or The Seven-Day Physical Activity Recall Questionnaire

Symptom Inventories

- Should include all case-defining symptoms including frequency and severity. We continually hear about severity. We often forget about frequency. They need to go together.
- Sleep can be addressed with Epworth and other standardized questionnaires.

- Pain scales

Additional Elements 2

Not all articles will need to deal with all additional elements. Some CFS researchers will not include, for example, things like brain, immune, or autonomic nervous systems. These will be included if the researchers focus on those particular areas. Although these elements might be much more expensive to collect, the group encourages the collection of those types of data.

Allergies, for example, should include specific IgE measurements or *in vitro* assessments of inhalant allergens such as pollens, molds, dust mites, and animal dander.

Much work still needs to be done

CFS researchers need to agree on the use of standardized and valid instruments. We hope that our work helps bring greater attention to this factor, promotes increased collaboration among investigators, and facilitates agreement on minimum standards for reporting findings. Our hope is that an article that is currently being written will be published.

Committee Discussion

Dr. Klimas: What advice do you have for researchers who are in the midst of their research, especially if it is a long-term project?

Dr. Jason: Those investigators should continue to publish those articles. One of the things that is going on in tandem with our efforts is an effort looking at domains of functioning and specific tests within those domains. Once that effort is done and we can recommend what we think are the best validated reliable instruments, we think that will help a next generation of investigators to begin coming together. We think that things like REDCap are also going to push things forward. We think that PROMIS [Patient Reported Outcomes Measurement Information System] is another interesting instrument that has been funded by NIH. There are all sorts of incredible advances going on in the field. What we want to do is encourage people to get aboard with those advances. Those folks who have not begun to do these things will probably begin to merge toward doing so.

Dr. Cook: It goes beyond the instruments. It is the detail of the reported methods. Even in some of the best research going on, the methods lack the detail for replication and extension. Hopefully this article will go a long way towards having researchers pay more attention to what they report about what they did in their science.

Dr. Michele: I would encourage you to include in your study designs data about the type of controls that were used as well as the blinding of those studies, recognizing of course that since the field is relatively young, you may not be doing the placebo-controlled, randomized, blind studies.

Dr. Dimitrakoff: I do think that this paper will provide the scientific basis for the recommendations that we are making. Looking forward, it will ensure that we are all on the same page and talking about the same patients. It is a great and honorable effort that will help move the field forward. Even looking

beyond that, it will probably provide us with more tools and a better structure for trying to target the right treatment to right patient as long as we know what patient population we are looking at.

Dr. Jason: This is really just a first step. There are multiple other steps that need to occur if we are going to move the field forward. But we have to start somewhere, and sometimes taking small steps is really the place to start.

Dr. Vincent: Is the information from this paper informing the research that CDC is now funding in the three clinical groups?

Dr. Jason: I think those are independent efforts. Ultimately, since there is some overlap in some of the individuals, one project might help inform the other project. The hope is that there will be dialog among these groups so that we can all learn from each other and continue improving our practice.

Dr. Vincent: How are you assessing your instruments?

Dr. Jason: There is a separate team that is working on domains of functioning. There are experts in those different domains who are making recommendations. For example, Dr. Lucinda Bateman came up with a recommendation for pain instruments as well as the PROMIS data set. We are now trying to decide which particular ones we want to recommend. We will try to get what we recommend on a system like REDCap so that investigators around the world can use them.

Dr. Unger: We did not try to reach consensus or recommendations on instruments. We are saying that you have to measure function in some way, and these are some current options. We did not think we could reach consensus on what the best instruments are at this point. There is a separate group that is trying to come to consensus about what best instruments are. Even then, it will not be absolute. There will be criteria that are used to evaluate instruments.

Dr. Lee: Many of us had not heard about the ICF until this morning. If that is relevant to the paper, it might be worth adding just to let others know that there is a standard way to collect information on disability.

Parting Words from CFSAC Members

Dr. Snell: This will be my last meeting here. I have been humbled by the commitment of the patients. I hope I can give just a small percentage of what they give to the illness. I will not be leaving CFS. I will be going back to looking at disability by studying post-exertional malaise. CFSAC has been a huge part of my life a long, long time and it is going to be difficult to leave.

Ms. Holderman: I just want to state for the record that the patient community and other stakeholders have requested that Drs. Snell, Klimas, and Jason remain on CFSAC for purposes of transition and continuity. I do not know if you would consider that or if CFSAC staffers would even extend that to you. I want to put in the record that those requests have come in.

Dr. Klimas: We have already extended a year so that there would be a staggering of people going on and off the committee. Right now you have everyone else rotating off CFSAC in 2014. You need to get some CFSAC members on an off-kilter cycle.

Dr. Lee: That is quite doable.

Dr. Klimas: I have been turning responsibility for the subcommittee that I chair to Eileen Holderman over the last six months. She is amazing. She is going to do a fabulous job. Since I have recycled onto this committee many times already, I am not going to say goodbye. I am just going to say, "See ya."

Dr. Jason: I am sorry I am not capable of saying a few words. I am an academic. But if I had to say a few things:

- There really have been some important things that have occurred over the last few years from the Research Subcommittee as well as the overall committee. We need to be able to acknowledge that. We certainly have a long way to go. You can sense the commitment of the new leadership at the CDC. The Research Subcommittee and the rest of the committee feel good about those types of changes that are beginning.

- Dr. Ron Glaser had some important influence on the number of SEP reviewers who have CFS expertise when he discovered that in the past; only 17% had ever published an article in the area. The new people who are overseeing the CFS SEP are ensuring that it reviews only CFS proposals. The people who are on that committee are better represented within the CFS community.

- The *ex officio* officers are being more responsive in giving us information. We no longer have to ask round after round of the same questions. We are now getting that information. There is no question that we have seen Dr. Lee, Ms. Bond, and others who have tremendous passion for this particular area of work. The change of leadership in ORWH again brings in a commitment and passion for this area.

- The patient community follows us closely, they care about what happens, and they want to be part of what we do. They want to testify. They want to see what we are doing. They want to interact with us by calling and emailing us. They think that we can make a difference. They have given their trust to us. The foundation of our country has to do with life, liberty, and the pursuit of happiness. These are fundamental, inalienable rights that the patients feel they have lost. We owe it to them; we have a commitment to them to make their lives better.

- Janet Smith said it the best in her testimony: "We need hope. We need help. We need it now. Not in five years, not in 10 years, but now.

CFSAC Subcommittee Reports

Education/Patient Care/Quality of Life Subcommittee

Dr. Klimas: The subcommittee talked about three broad areas: the ICD 10 presentation, the DHHS working group and its mission, and thoughts from Alaine Perry about how to use new technologies to expedite the learning curve in effective therapies.

Regarding ICD-10, Option 1 is the best of the options. We need to be lumpers rather than splitters on the terminology of ME/CFS and post viral fatigue syndrome, with the idea that we are moving toward a

name change. The change is not likely to be multiple names with multiple divisions. We are going to have ICD-10 around for a long time. If we could put things under a single code, I think we will be more successful in our name change efforts.

Mr. Krafchick presented the subcommittee's first recommendation:

Recommendation 1

1) The Chronic Fatigue Syndrome Advisory Committee (CFSAC) considers CFS to be a multi-system disease and rejects any proposal to classify CFS as a psychiatric condition in the U.S. disease classification systems.

2) CFSAC rejects the current classification of CFS in Chapter 18 of ICD-9-CM under R53.82, Chronic fatigue unspecified, chronic fatigue syndrome, not otherwise specified.

***3) CFSAC continues to recommend that CFS should be classified in ICD-10-CM in Chapter 6 under Diseases of the Nervous System at G93.3 in line with ICD-10, the World Health Organization, and ICD-10-CA, the Canadian Clinical Modification and in accordance with CFSAC's recommendations of August 2005 and May 2011. CFSAC rejects the National Center for Health Statistics Option 2 and recommends that CFS remains in the same code and the same subcode as myalgic* encephalomyelitis because CFS includes both viral and non-viral triggers.**

4) CFSAC recommends that an "excludes one" be added to G93.3 for chronic fatigue, R53.82, and neurasthenia, F48.8. CFSAC recommends that these changes be made in ICD-10-CM prior to its rollout in 2013.

Dr. Klimas seconded the motion. **Dr. Jason** called the question.

CFSAC voted unanimously to approve Recommendation 1.

Dr. Klimas noted that one area discussed by the Patient Care/Quality of Life Subcommittee was encouraging the concept of a true DHHS interagency working task force on CFS. The following recommendation addresses this concept:

Recommendation 2

The Chronic Fatigue Syndrome Advisory Committee (CFSAC) would like to encourage and support the Interagency Working Group and ask this group to work together to pool resources that would put into place the mission of the "Centers of Excellence" concept that has been recommended repeatedly by this advisory committee. Specifically, CFSAC encourages utilizing DHHS agency programs and demonstration projects that are available through the various agencies that would develop and coordinate an effort to support innovative virtual and physical platforms that facilitate evaluation and treatment, research, and public and provider education. Outreach and access to underserved populations, including people who do not have access to expert care, should be a priority in this effort.

Dr. Klimas provided some background on subcommittee development of the recommendation. The DHHS working task force needs a mission, she said, and the centers of excellence are all about making healthcare and expert providers accessible to patients and integrating this into research platforms that

move the field forward. Dr. Klimas reported that **Ms. Perry** made available a presentation from her agency on how an assessment platform would help develop the evidence needed for evidence-based interventions. Recommendation 2 charges the DHHS task force with a clear mission, which is to pull together agencies resources that could be cobbled together into a program that would answer the needs of the patient population.

Mr. Krafchick added that "cobble together" also means find the funds in a variety of different places to start a couple of centers of excellence in the United States.

Dr. Jason seconded the recommendation.

Discussion

Dr. Levine: This recommendation differs from previous recommendations about centers of excellence because we are making use of our *ex-officios* and the resources of this committee. I have been very impressed at the last couple of committee meetings at how the *ex officios* have really stepped up to the plate and offered us their services and some of their innovative tools. I think the centers of excellence were at first thought of as buildings where professionals and specialists in this area would meet. What the *ex officios* have offered us is an opportunity to use virtual tools to extend the services and expertise that we can provide to underserved populations. I want to emphasize the interagency portion because I think it is important for the centers of excellence recommendation to work.

Dr. Snell: My understanding is that we are recommending to the Secretary that she charge the agencies within DHHS to work together within their various structures to put together something that resembles a center of excellence.

Dr. Klimas: With very innovative thinking, a center could be a virtual platform that we can all access or it could be numerous demonstration projects that come together under an umbrella.

Dr. Snell: So we are not proscribing what centers should look like?

Dr. Klimas: Right. We want people to be very creative in looking into their agencies. This could extend beyond DHHS to borrow from the Departments of Labor or Education or someplace else.

Dr. Snell: Does the recommendation incorporate some mechanism for CFSAC to be involved?

Dr. Klimas: We discussed that we would be happy to attend the task force meetings and offer expertise and motivation.

Mr. Krafchick: It was impressive hearing about the Echo Program that already exists and the model that was used for hepatitis C. It was obvious that something like that could be extended. The question then became who gives the Echo to the primary care providers? The centers of excellence would be a way of coordinating people.

Dr. Jason: There is a general consensus that this is a fantastic idea. The specific wording of it can be detailed after this meeting. For our purposes right now, I see no objections to it. Clarification will happen as it gets written. I'd like to call the question.

Dr. Snell took a vote and CFSAC voted unanimously to approve the recommendation.

Dr. Lee noted a November 18, 2011 deadline for filing comments for ICD-10-CM. She suggested that Dr. Snell send Recommendation 1 to Dr. Pickett via email before November 18. They agreed on this course of action.

Research Subcommittee

Dr. Jason noted that a new NIH PAR [Program Announcement with special receipt, referral, and/or review considerations] is in the offing, but it is unclear whether it will include clinical trials. With that in mind:

Recommendation 3

CFSAC recommends to the Secretary that a Request for Applications (RFA) be issued for clinical trials for ME research.

Dr. Cook seconded the motion.

Discussion

Dr. Levine: Someone from NIH has mentioned that bench to beside clinical trials could be initiated if it was a collaboration between intramural and extramural.

Dr. Jason: Just to clarify, we are not saying anything against the PAR. We think it is important to get out there. We are recommending an RFA in addition to the PAR.

Dr. Marshall: Just for clarification, I think that Dr. Clayton said this is an intramural/extramural collaboration. It is initiated intramurally, not through a PA. [Dr. Clayton confirmed this and offered to connect CFSAC members with the appropriate contact.] You contact the intramural investigator, you propose something, and you work through NIH requirements to create an intramural/extramural collaboration. It is peer reviewed through the intramural process [confirmed by Dr. Clayton.]

Dr. Klimas: My following comment is directed toward NIH. When the CFIDS Association of American (CAA) had their call for proposals for their very small pot of money (about $120,000), they had 28 proposals. There is something essentially broken if the NIH is saying that it is getting 16 proposals. There are significant barriers there. When NIH had an RFA with a $4 million set-aside, the agency got more than 30 responses. I strongly urge NIH to put on its thinking cap and consider what is wrong when a small foundation can get more responses to an RFA than NIH can.

Dr. Clayton: We are doing that, but I would like to know what your ideas are. This has to be done in partnership. People need to be putting applications in for us to be able to show that there is a need for more funding. I would like to know from you where you see the barriers. You are out there in the field and hear what people are saying. The investigators are much closer to you.

Dr. Klimas: The answer is complicated, but part of it is rejection. There has been a lot of rejection and people do not come back if they are rejected multiple times. We may have lost some early enthusiasm. People think that they are not as likely to get a fundable score by NIH as they might get from a foundation. How can we make that better? CAA can only accept one or two projects. That means there are going to be 25 rejections. Those are all R21s. How do we get those 25 projects into NIH's next cycle?

Dr. Clayton: Those foundation applications are already prepared, so they should be able to be recast.

Dr. Klimas: Maybe you might like to try something innovative such as compose a letter that CAA can send out along with their rejections. Investigators would receive an NIH application packet instructing them how to turn their application into an R21.

Dr. Lee: It sounds like you [Dr. Clayton] need a focus group. There are only 28 investigators. You could informally talk to those 28 investigators and see if you can figure out what the barriers are.

Dr. Klimas: Many of the proposals are clinical trials for which there is no avenue for submission. Investigators were discouraged from submitting them in the language of the former PA.

Dr. Clayton: The funding rate is actually higher in CFS than in other areas. This is not an issue unique to CFS. It is a problem keeping investigators in research and encouraging new researchers in any scientific discipline. As a scientific and academic community, if we want to build a knowledge base and move it forward, we are going to have to be creative and work together in partnership to cooperate in new ways. Funds are limited for everyone.

Dr. Jason: We have three examples to support the idea of RFAs for clinical trials. The NIH's RFA that was put out after its State of the Science Meeting about six years ago generated more than 35 proposals. The CAA has done RFAs twice and generated some fantastic proposals. I say to myself, "Why are these not coming to NIH?" The thing that differentiates NIH's RFA from six years ago and the two CAA rounds was that they said, "We have a pile of money that we are giving away." That brings in applications like nothing else.

Dr. Snell noted that this discussion would not directly impact the recommendation and in the interest of time, called the question.

CFSAC voted unanimously to approve the recommendation.

Recommendation 4

This recommendation addresses the process by which CFSAC transmits recommendations to the Secretary and the Secretary communicates back to CFSAC whether or not its recommendation was followed. CFSAC recommends that this process be clarified and articulated so that it can be transparent.

Dr. Jason said that the purpose of the recommendation is to try to firm up a nebulous, ambiguous process.

Dr. Cook seconded the motion.

Dr. Snell called the question.

CFSAC voted unanimously to approve the recommendation.

Dr. Jason noted that the Research Subcommittee was impressed with the ICF presentation. His panel suggests that the *ex officios* take this seriously. It is very promising. If there is any way that some of this work can spill over into the ME/CFS arena, it could enrich not only what is going on with ICF but also research and patient care the ME/CFS field.

Dr. Marshall said that he is glad to walk in Dr. Jason's footsteps and complimented Dr. Jason for being a pioneer who thinks of things comprehensively. Dr. Marshall said that the subcommittees are going to take directions from the committee, then hammer out ideas in their separate arenas, recognizing that there is some overlap between subcommittees and hoping that collaboration will make CFSAC more effective. Dr. Marshall expressed hope that Dr. Jason can return as an *ex officio* advisor. Dr. Marshall said that Dr. Jason's passion for his work is matched only by his intelligence.

Dr. Snell emphasized the value of the leadership meetings that occur between CFSAC meetings, noting that the subcommittees can discuss and smooth out any areas of overlap.

Dr. Snell explained that the CFSAC chair is chosen by the DHHS Secretary but that the committee can forward a name for her consideration. Two people expressed interest in taking over the chair. A secret ballot was conducted over summer 2011. Mr. Krafchick received the most votes.

Dr. Marshall expressed appreciation for Dr. Jason's recognition that taking a leadership position on CFSAC requires a learning curve.

Dr. Marshall: I started in May 2010 and am now at the point where I feel comfortable taking the lead on the Research Subcommittee. It has taken about a year and a half. It would be a nice idea to forward to Secretary Sebelius the idea of allowing the identification of a chair-elect or sub-chair elect far enough in advance that he or she can be brought up to speed. There has been a real value for me in being on calls over the past year and a half as the subcommittee chair-elect. I would encourage us to let Secretary Sebelius know that for us, it is an extremely useful process to identify committee and subcommittee chairs far enough in advance to have continuity of leadership.

Dr. Snell: This would be possible for subcommittee chairs because CFSAC selects the people for those positions. The Secretary selects the CFSAC chair. I found out three weeks before my first meeting that I would be the chair.

Mr. Marshall: Then I will put it in the form of a recommendation that the DHHS Secretary select a CFSAC chair-elect with at least a year of overlap to give that person a chance to come up to speed and provide continuity of leadership. The chair-elect could be involved in between-meeting calls and interactions with Dr. Koh. This recommendation would be subject to any Federal statutes or regulations regarding the CFSAC chair. If it is not allowed, then strike it down.

Mr. Krafchick: I would second that. I am very honored to be recommended to be the chair and am delighted to assume that responsibility, but I recognize that being a part of whatever goes on between

meetings would be useful to anybody moving forward. That is not to say that I could not learn fast enough to pick up the flag and carry it, but I think this is a good idea.

Dr. Jason: I suggest that Mr. Krafchick be given a courtesy invitation to the leadership meetings that will occur over the next six months and include the co-chairs of the CFSAC subcommittees, Dr. Lee, Ms. Bond, and Dr. Koh (by invitation). Mr. Krafchick can watch the process, be involved in it, and if it turns out that he becomes the chair, he can assume the role with that pre-history.

Dr. Snell and Dr. Lee confirmed that a formal recommendation is not needed for Mr. Krafchick to attend leadership meetings. Dr. Klimas pointed out that the current subcommittee chairs do not rotate off until April 2012 and would be attending the leadership meetings and conference calls.

Dr. Klimas opened a discussion of the new DHHS CFS task force, including how Dr. Lee and Ms. Bond think it might work and what CFSAC can do to help. Dr. Klimas noted that there is a very steep learning curve during the first or second meeting of a new group. She said that CFSAC subcommittees have learned how to get work done between meetings and she is thrilled that CFSAC *ex officio* members are now taking actions between meetings.

Dr. Snell exited the meeting and Dr. Klimas sat in as CFSAC chair for the rest of the meeting.

DHHS CFS Working Group

Dr. Lee: This is still a work in progress. The process was begun out of the Office of the Secretary. We found out about it after it had been going on for several months and we have been involved in it ever since. There has been a preliminary and currently incomplete inventory of things that various agencies are doing in CFS. There is a table that shows this. There are draft steps to be taken. There will not be a published document. The end result is going to be some strategy steps and some action steps. There is a draft memo that is currently planned to come from one of the Secretary's four counselors. The memo will be sent to the heads of the DHHS agencies outlining the working group process and asking them to appoint an individual to participate in the group who is sufficiently high level to make decisions on behalf of the agency. If any CFSAC *ex officios* are chosen as participants, they will have to be high-level enough to make decisions.

This is a process that is anticipated to include just three to five monthly meetings. There then may action steps to continue. Dr. Lee will chair the group. The action steps will be posted on the CFSAC website. Dr. Lee said that CFSAC has already helped her by what she has learned in two days of meetings. She encouraged CFSAC members to feed her ideas. She added that the *ex officios* are going to be extremely important to this process as well.

Past Recommendations

Dr. Lee: Some of them are way out of date. Some of them are essentially the same recommendations worded in different ways. We could do some work on these in the next month or two with subcommittee calls. When presenting material to high-level people, you have got one page and if you cannot say what you want them to learn in about in one page, you are saying too much.

Dr. Marshall: Those of us who write R applications have that experience. If we cannot get it in the first page, it is a waste of time. A summary first page does not preclude more information, but the support information must be labeled as such.

Dr. Lee: To clarify, I meant that all CFSAC recommendations should go on one page, not one page per recommendation.

Mr. Krafchick: If we had to limit it, I would say look at the recommendations that were put forth today. They are the most current and the ones that would make a difference immediately. I do agree that we have to take a look at the other ones. As I remember, they are categorizable. For example, all the ones related to the centers of excellence really are subsumed in what we did today.

Dr. Lee: I would advise you to go with everything you can fit on a page. I think that you can get more than three or four or five recommendations on one page.

Dr. Klimas: I am going to recommend that the subcommittees all meet in early December by conference calls and make prioritizing these recommendations your primary task so that we can get this information to the DHHS task force in a timely fashion. Task force meetings will begin very soon and we need to help. Individually, if members have recommendations that would help the process, send them forward. You do not have to work through the subcommittee structure.

Dr. Jason: We are the representatives of various constituent groups and we talk for them. It is important to prioritize the recommendations. Is there any precedent for bringing other groups into this process who might be able to look at the recommendations and give us feedback? If there is any way of doing that during these critical times, it would bring a fantastic inclusionary perspective.

Dr. Lee: This is not my process. At the moment is it three or four meetings. I would be a little leery about doing what you are talking about too soon. We are still figuring out what we are going to do. If we continue in some way past current plans, then I think you have an excellent idea.

Dr. Klimas: There is nothing that stops the advocacy community and other stakeholders from contacting members of the CFSAC subcommittees so we can bring your ideas forward. It may not be a formal mechanism through Dr. Lee's office, but it would be a very reasonable use of CFSAC members.

Dr. Lee: We have a CFSAC website with an email box. People could send recommendations there as well. I would really prefer them not to go to my email box. I cannot tell you how hard it is to manage my inbox. We look at the CFSAC inbox a lot.

Dr. Jason: Most people are not going to look at the 50 past recommendations. If we were to distill 25 of them, put them on the website, and ask for comment on which are the most important ones, we could potentially get some feedback from a larger audience.

Dr. Klimas: I think we are going to get feedback from a larger audience no matter how we choose to do this. We will read them and try to be thoughtful. I do not see distilling subcommittee priorities to one page as a hard job. I think we know what we need to do already.

Dr. Lee: Twenty-five is too many recommendations. Prioritization is really the subcommittees' job. When you get this done, we can post it on the CFSAC website.

Dr. Klimas: The past recommendations are really redundant. The centers of excellence appear in there many, many, many times in one iteration or another. I am going to cheer for the centers of excellence as the number one priority of this group because it ultimately affects many other issues—lack of expert physicians to treat patients, lack of care, and no evidence-based guidelines because the evidence has not been collected in a way that we can deliver the goods.

Dr. Jason: Our different subcommittees can work on this, but we can also work on it together to facilitate this process. The more we are talking among ourselves, the better chance we have of getting it done.

Dr. Lee confirmed that anything labeled a CFSAC recommendation must be voted on in an open committee meeting, but anyone can send her ideas for the task force. **Ms. Holderman** gave the example of the memos she has sent Dr. Lee listing advocate and stakeholder concerns.

Dr. Klimas gave *ex officio* members an opportunity to present ideas to CFSAC voting members on how they could help the *ex officios* move their agendas forward in their various areas:

Dr. Clayton welcomed ideas for working together in new ways within current budget constraints. She challenged CFSAC members to come up with ways to work strategically. She said a key point is to get new early stage investigators into the field. She suggested that CFSAC members individually mentor investigators.

Dr. Cook: The lull in investigators can be partially explained by NIH deciding not to renew the centers. This sent a strong message to the CFS scientific community that NIH is not as supportive of the research. A lot of investigators went in different directions. The State of the Knowledge Workshop has investigators dusting themselves off and getting up off the canvas. NIH should not use the old notion that there is not an interested scientific community. I do not expect the number of research applications to remain low. Having RFAs and some encouragement and incentive from the funding side will help that process.

Dr. Marshall: I am Vice Chairman for Research for the Medicine Department at the University of Mississippi. One of the challenges we have is between the basic scientists and the clinical scientists. There is a scare over funding. The NIDDK just announced that it is not participating in the parent R21 program anymore. Several program officers have advised telling young investigators not to apply for R21s. The young investigators are then told that they do not have a CV strong enough to apply for an RO1. Some of us who have been through these yin/yang cycles view it as playing the lottery. Maybe the odds are not very good, but they are zero if you do not play. But there is the view that it is a waste of time to apply to NIH right now unless you are already an established investigator. That is what is keeping young people away in large numbers, not just from ME/CFS research. I think we can help people get over that hump of thinking they are wasting their time. They are not, even if they do not get funded, because every application I have ever written has helped me write a better one later on.

Ms. Holderman suggested using social networking to attract young investigators.

Dr. Clayton: Deputy Director of Extramural Research Sally Rockey has a blog called “Rock Talk” and a lot of young investigators follow her blog. That is one strategy that is already in place, but I will take your suggestion back.

Ms. Holderman: Perhaps you could be even more interactive. I know that when the XMRV issue was really hot, everyone was hopping onto the virology blogs. It was a fascinating place to go and listen in. It attracted a lot of different people.

Dr. Klimas: Physician scientists often see themselves as second class scientists because they have to spend a lot of time in the clinic in addition to doing research. One of the missions of the Veterans Administration hospitals has been to support physician scientists. It happens to be a very friendly place to get for young investigator, midlife, and later career development types of awards as well as independent research tracks. I encourage you if you are mentoring young MDs to get them 5/8 appointments at the VA so they are eligible to apply for funds in general and career development awards in particular.

Dr. Jason: One of our big challenges is how to work together as networks. We have lots of common interests. Using similar strategies and instruments will help that. But there is also something called REDCap that brings together researchers from all over the country and the world. It gives the possibility of using common instruments, potentially building larger databases. If we are really going to make a lot of progress in this area, we need samples that are larger than 30, 40, 50 patients. The variations that occur within this illness are extreme, and if we could get thousands of people in databases with well-described characteristics that could really push the field forward. Some of that is beginning to happen. The question is how do we make partnerships with all of these different entities so that they are all dialoging together?

Dr. Vincent described the Rochester Epidemiology Project, which has a CDC contract, is tracking people from birth to death, and is interfacing EMR [electronic medical records] with REDCap. There have been cohorts built on many chronic disease conditions. The project has characterized CFS and controls. The work has not been peer-reviewed yet, so details are not available.

Dr. Klimas: For the record, REDCap is an NIH-funded platform that is nationally and internationally accessible to house data systems. For example, you might be able to pull down the SF 36 and a number of others into the menu of things you are asking your patients or your subjects. You can take a minimal panel down and have that as a base amount of information that you are collecting. You can then increase it with your own instruments. You can use the instruments that are already up and running and are universal.

Dr. Vincent noted that REDCap was not funded by NIH; it came from Vanderbilt.

Dr. Dimitrakoff: REDCap is a platform that was originated at Vanderbilt. We used REDCap in collaboration with Dr. Jason and Dr. Klimas for the first time that it has been used uniquely for CFS. We used REDCap through the resources that are provided through the Harvard Catalyst at Harvard Medical School. The Harvard Catalyst is a big translational research project that provides administrative support through an NIH grant to Harvard Medical School. The software for the REDCap platform, however, originated at Vanderbilt. The best thing about REDCap is that it creates a place where people from different institutions can come together, share patient cohorts and data, and at the same time look at biomarkers or different instruments. The participants do this in a way that protects the privacy of the patients. It is HIPAA-compliant. You can create a large virtual patient cohort and you can look at as many variables as you want.

Dr. Klimas: I thought that Vanderbilt got funding from NIH.

Dr. Jason: Although you need some administrative support for it, REDCap is free. There are thousands of investigators around the world that are using it right now. At Harvard, there are 240 projects that are going on with REDCap.

Dr. Klimas: Ms. Perry and I in the subcommittee were talking about innovative ways of using this to create a rapid learning program to help us better understand interventions and their impacts on our patients.

Ms. Holderman: I am hoping that CFSAC staff will consider extending the terms of Drs. Snell, Klimas, and Jason. I know if you do not return officially, you are going to stay committed. I would like to publicly thank Drs. Snell, Klimas, and Jason.

Ms. Holderman related her favorite stories about Drs. Jason and Klimas from a CFS conference in Seattle 10 years ago. Dr. Jason suggested that members of the government, advocacy, and scientific realms have lunch together. The suggestion raised eyebrows at the time because stakeholders did not interact as much as they currently do. She concluded that Dr. Jason is still working to foster collaboration in the CFS field.

Ms. Holderman described her image of Dr. Klimas leaving the same conference, wheeling her suitcase behind her in the rain. Ms. Holderman said that the image evokes Dr. Klimas's unbelievable dedication to the CFS field then and now.

Dr. Klimas: We are going to be leaving you in very good hands between Ms. Holderman and Dr. Marshall running the two subcommittees. I look forward to seeing the committees' progress. Mr. Krafchick, if you end up being the super cheese that would be very cool. I can see things going very smoothly. You are an organized and motivated person.

Mr. Krafchick: This is my fourth meeting. It has been an amazing experience so far and I can see what looks like an upward trend in the ability to get things accomplished, which is very rewarding. I am going to miss you and Dr. Jason and Dr. Snell because you have been, in a lot of ways, the heart and soul of the group. Maybe we will clone a new heart and expand the soul, but you will be missed if you cannot stay.

Adjournment

Dr. Klimas adjourned the meeting.