

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



Hubert H. Humphrey Building, Room 800, 200 Independence Avenue, SW
Washington, DC 20201

Wednesday, October 13, 2010 – 9:00 am to 5:15 pm

and

Thursday, October 14, 2010 – 9:00 am to 4:30 pm

Voting Membership

Name		Term
Chairman Christopher Snell, PhD	Stockton, CA	04/01/07 to 04/01/11
Dane B. Cook, PhD	Madison, WI	05/10/10 to 05/10/14
Ronald Glaser, PhD	Columbus, OH	04/01/07 to 04/01/11
Arthur J. Hartz, MD, PhD	Iowa City, IA	04/01/07 to 04/01/11
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 04/01/11
Steven P. Krafchick, MPH, JD	Seattle, WA	07/01/10 to 07/01/14
Nancy Klimas, MD	Miami, FL	04/01/07 to 04/01/11
Susan M. Levine, MD	New York, NY	05/10/10 to 05/10/14
Gailen Marshall Jr., MD, PhD	Jackson, MS	05/10/10 to 05/10/14

Ex Officio Membership

Centers for Disease Control and Prevention

J. Michael Miller, PhD (*Primary*) – Associate Director for Science, National Center for Zoonotic, Vector-borne, and Enteric Diseases

Food and Drug Administration

Marc W. Cavaille-Coll, MD, PhD – Medical Officer Team Leader, Division of Special Pathogens and Immunologic Drug Products

Health Resources and Services Administration

Deborah Willis-Fillinger, MD (*Primary*) – Senior Medical Advisor, Office of the Administrator, Center for Quality

National Institutes of Health

Eleanor Hanna, PhD (*Primary*) – Associate Director for Special Projects and Centers, Office of Research on Women's Health

Dennis F. Mangan, Ph.D. (*Alternate*) – Senior Research Advisor, Office of Research on Women's Health

Social Security Administration

Cheryl A. Williams (*Primary*) – Acting Director, Office of Medical Listings Improvement

Mike O'Connor (*Alternate*) – Supervisory Team Leader, Office of Medical Listings Improvement

Agency for Healthcare Research and Quality

Christine Williams – Director of Strategic Partnerships

Centers for Medicare and Medicaid Services

Alaine Perry – Senior Advisor, Center for Strategic Planning

EXECUTIVE SECRETARY / Designated Federal Official

Wanda K. Jones, DrPH – Principal Deputy Assistant Secretary for Health, Office of the Assistant Secretary for Health

Agenda Wednesday, October 13, 2010

9:00 am	<u>Call to Order</u>	pg 6	Dr. Christopher Snell <i>Chair, CFSAC</i>
	<u>Opening Remarks</u>		
		pg 6	Dr. Wanda Jones Designated Federal Official
	<u>Roll Call, Housekeeping</u>		
		pg 6	Dr. Howard K. Koh
	<u>Statement from the Assistant Secretary for Health</u>		
9:30 am	<u>Cognitive Functioning in CFS</u>	pg 8	Dr. Gudrun Lange
10:15 am	Committee Discussion	Pg 10	Committee Members
10:45 am	<u>Public Comment</u>	pg 13	Public
11:45 am	Subcommittee Lunch		Subcommittee Members
1:00 pm	<u>Functional Capacity Evaluation</u>	pg 17	Dr. Ted Becker
	<u>Vocational Evaluation</u>		Kathy Reid
	<u>Metabolic Evaluation</u>		Dr. Chris Snell
2:15 pm	<u>SSA presentation on Improving Disability Assessment Process</u>	pg 20	Mike O'Connor Social Security Administration
2:45 pm	<u>DOL/ERISA presentation</u>	pg 23	Elena Lynett Senior Health Law Specialist, Employee Benefits Security Administration's Office of Health Plan

			Standards and Compliance Assistance, Department of Labor
3:15 pm	<u>Health Care Reform—Impact on Persons with CFS</u>	pg 25	Mayra Alvarez Director of Public Health, Department of Health and Human Services, Office of Health Reform
3:45 pm	<u>Committee Discussion</u>	pg 25	Committee Members
4:15 pm	<u>Public Comment</u>	pg 27	Public
5:15 pm	<u>Adjourn</u>	pg 32	

Agenda Thursday, October 14, 2010

9:00 am	<u>Call to Order</u> <u>Opening Remarks</u>	pg 33	Dr. Christopher Snell <i>Chair, CFSAC</i>
	<u>Roll Call, Housekeeping</u>	pg 33	Dr. Wanda Jones Designated Federal Official
9:15 am	<u>Science Day - Key Points and Discussion</u>	pg 34	Committee Members
10:15 am	<u>Extramural CFS Research at NIH</u>	Pg 38	Program Officials from Trans-NIH Working Group
11:15 am	<u>Agency Progress on Recommendations</u>	pg 45	Ex Officio Agency Representatives
12:00 pm	Subcommittee Lunch		Subcommittee

1:00 pm	<u>Public Comment</u>	pg 47	Members Public
2:00 pm	<u>Committee Discussion: Finalize Recommendations</u>	pg 53	Committee Members
4:30 pm	<u>Adjourn</u>	pg 62	

The following document contains highlights of the Chronic Fatigue Syndrome Advisory Committee (CFSAC) Meeting held on October 13-14, 2010. Access a webcast of complete meeting proceedings at: <http://www.hhs.gov/advcomcfs/>.

WEDNESDAY, OCTOBER 13, 2010

ROLL CALL

Dr. Jones conducted roll call with the following results:

Present: Dr. Christopher Snell, Dr. Ronald Glazer, Dr. Arthur Hartz, Ms. Eileen Holderman, Dr. Michael Houghton, Dr. Leonard Jason, Mr. Steven Krafchick, Dr. Nancy Klimas, Dr. Susan Levine, Dr. Gailen Marshall, Dr. Dane Cook.

Ex officio members Present: Christine Williams, Dr. Michael Miller, Ms. Alaine Perry will be arriving momentarily, Dr. Marc W. Cavaille-Coll and Mr. Mike O'Connor arrived later.

Absent: Dr. Deborah Willis-Fillinger, Dr. Eleanor Hanna, Dr. Dennis F. Mangan, Dr. Tracee Treadwell, (Alternate), and Ms. Cheryl Williams.

CALL TO ORDER/OPENING REMARKS

Dr. Wanda Jones

- Remarked that issues with Metro may make some attendees late.
- Noted the need to keep to a tight schedule as a courtesy to web viewers. Speakers have an allotted time period. There will be three public comment periods over the two days. Noted the arrival of Ms. Alaine Perry from the Center for Medicare and Medicaid Services.
- Introduced Dr. Howard Koh, Assistant Secretary for Health.

WELCOME STATEMENT FROM THE ASSISTANT SECRETARY FOR HEALTH

Dr. Howard Koh, Assistant Secretary for Health, U.S. Department of Health and Human Services

- Welcomed all members to the committee and thanked them for their "expertise, dedication, and willingness to serve."
- Noted the need for work in this vital area, given the number of people suffering from CFS (Chronic Fatigue Syndrome).
- Commended Dr. Snell for chairing the committee and his valuable work in the area over his career. Also thanked Dr. Jones for her effort and work to advance CFSAC issues.

- Noted the quality of experts that have been brought in to present and discuss and looked forward to progress on the numerous challenging questions surrounding CFS after “vibrant discussion” on the previous day’s meeting.
- Stated that the Charter for the Advisory Committee was approved for two additional years by the Secretary on September 5, 2010.
- Remarked on progress on half of the recommendations the Committee has made since 2004. Recommended everyone access the public tracking document on the CFSAC website.
- Remarked on success of scientific discussions surrounding CFS, notably the National Institutes of Health’s (NIH) first international workshop on XMRV (Xenotropic murine leukemia virus-related virus) last month.
- Noted disability coverage and assessment questions that also were up for discussion, particularly the impact of the Affordable Care Act (ACA).

Dr. Jones

- Pointed out that a copy of the Charter for the advisory committee was online and also located in the back of the room. Bylaws are still in process and will be finalized and posted as soon as possible after the meeting.
- Nominations are being accepted for upcoming committee vacancies. They have developed a plan for a two to three member turnover annually for more continuity.
- Advocated one year extensions for the Chair and subcommittee Co-chairs to achieve the plan to stagger committee memberships.
- Noted improvements to the U.S. Department of Health and Human Services’ website, including future integration of historical notes, and significantly improved traffic to the CFSAC, especially for webcasts.
- Turned the meeting over to the chair.

MINUTES APPROVAL

Dr. Leonard Jason moved the minutes from the previous meeting be approved, with the modification to the Charter to include the term ‘etiologies’ in the description of duties section. The minutes from the last meeting were seconded and approved.

Dr. Jason asked Dr. Snell if there would be an opportunity to have dialogue with Dr. Howard Koh in some format, and asked whether the recommended increased contact between the two has been actualized. Dr. Snell admitted he hasn’t had much contact and recognized this was an issue. He mentioned a conversation with Dr. Koh, who

stated he would welcome an appointment to talk. Dr. Jones mentioned they did have a phone call last week with Dr. Koh. Dr. Snell said he would ask Dr. Koh if he would be willing to join in on conference calls with a view to improving access.

Dr. Christopher Snell

- Highlighted significance of these meetings to the CFS community, and noted that programming is very deliberate for the meetings.
- Remarked on yesterday's symposium on scientific issues, saying it "raised more questions than it answered".
- Remarked on the variance in research and many different intersections of research showcased in yesterday's meeting, which confirmed the need for improvement on:
 - The mechanisms for the limited number of researchers to collaborate and share results, protocols, and studies
 - Patient selection criteria
 - Common objective measures to evaluate symptoms
 - Mechanisms for implementing clinical trials
 - Identifying triggers or stressors to make symptoms present for better research
- Remarked that while the science discussion is relevant to today's meeting, much of the concern he experiences from those with CFS is not concerned with the science but more the practical concerns of access to care, and disability and healthcare issues. These will form the focus of the program today.
- Introduced their first speaker, Dr. Gudrun Lange, Professor, Department of Physical Medicine and Rehabilitation, UMDNJ-NJMS (University of Medicine and Dentistry, New Jersey-New Jersey Medical School). Her area of specialty is cognitive functioning, and she will share the current objective knowledge available on the subject of "Brainfog".

COGNITIVE FUNCTIONING IN CFS

Dr. Gudrun Lange, Professor, Department of Physical Medicine and Rehabilitation, UMDNJ-NJMS

- Reviewed her 15-year history working on the neurological underpinnings of CFS, especially in the context of assessing patients for disability application. Today she will focus on Social Security issues.

- Outlined discussion topics on cognitive functioning in CFS, giving examples and detail in each area. Patients perceive that cognitive problems or “brain fog” are disabling.
- Noted cognitive symptoms are most commonly concentration and attention problems, memory difficulties, difficulty finding words, and an inability to think. These symptoms, especially as they lead to patients perceiving they are dementing, are detrimental to self worth and often result in isolation.
- Focused on mismatch between subjective reports and the objective data required for claim corroboration. It can be difficult for researchers to provide findings to support disability claims.
- Compared Dr. Fred Friedberg’s research published using 16 years of data showing the increase in funding for neuroimaging versus neuropsychology research.
- Illustrated diminishing neuropsychological research and increase in neuroimaging, which is problematic for the non-researcher. Neuroimaging is still experimental, difficult to interpret, and not often accepted as evidence, as study conclusions conflict. It is also very expensive for patients. Functional testing produces more actionable data.
- Stressed that clinicians need to be better educated about CFS. Claims that are denied by Social Security Administration (SSA) are usually due to a poorly documented cognitive evaluation.
- Agreed with Dr. Snell’s call for stratification of patient data, better method with control groups, standardized tools of analysis, and separating out those with other overlapping conditions.
- Outlined different methodologies in neuroimaging studies, the results for which, on the clinical side, can be confusing. These methodologies point to CFS as a systemic problem, not isolated to any one brain region. These methodologies include:
 - Static Neuroimaging: Brain Lesions and Brain Volume
 - Dynamic Neuroimaging: Relative and Absolute Cerebral Blood Flow
 - Metabolic Studies: Positron Emission Tomography, Magnetic Resonance Spectroscopy
 - Functional Neuroimaging: These tests challenge working memory system. These are most encouraging and support symptoms that are expressed by patients. Most notably, studies show that when taxed by complex tasks, certain brain regions of CFS patients have smaller or even no activation. Notably, these studies suggest that CFS patients exhibit the same behavior in terms of effort on these tests, they do not amplify their symptoms or malingering with any great frequency.

- Commented that the most consistent finding is impaired information processing, especially processing of complex information. It is this that should be focused on in examination. This information should be looked at relative to normal intellectual function, not used in an absolute sense.
- Noted people are likely to notice deterioration of their fragile higher level functioning, and multitasking, as this is the “edge” noticed by others, rewarded by society, and necessary in the workplace. This functioning is not easily regained, but can be improved.
- Stressed Social Security Disability Act parameters mean that even if a patient has symptoms consistent with CFS, they do not qualify unless they are considered severe enough. The documentation of the diagnosis is nowhere near as significant as documentation of the limitations the diagnosis imposes.

This concluded Dr. Lange’s presentation.

COMMITTEE DISCUSSION

Dr. Gailen Marshall noted that many of his colleagues who see patients with CFS say they cannot find anything wrong with them. He wondered if Dr. Lange finds the same to be true with her colleagues, and is startled both by the fact we don’t see commonly reported symptoms born out in objective findings by those in the psychological field, and how little acceptance there is of the condition.

Dr. Lange stated most physicians look for absolute findings. Instead, there is a need to educate neuropsychologists about the illness in terms of what signs to look for relative to information processing, so they will run a more sophisticated array of tests, not just use a technician to run normal testing batteries.

Dr. Jason posed the following questions: Do you feel social security adjustors are fair? What types of recommendations would you make? Are there enough trained professionals? What can the Advisory Committee do to help education? Where do we go to help individuals in finding rehabilitation? Are there enough trained people? Do you think we are facing a crisis in this field with lack of service?

Dr. Lange believes the adjusters are bound by regulation, which can be alleviated by education. Education has to start in graduate school. After seeing a patient, remediation is something that can help, even if it doesn’t solve the issue but rather affords coping mechanisms and adjustments.

Dr. Lange also argues the Centers for Disease Control and Prevention (CDC) could do more to alleviate the lack of education through various media including the internet. Neuropsychological evaluations are expensive, and Medicare and Medicaid reimbursement would help. It needs to be easier for a patient to see a neuropsychologist. She noted that by the time patients come to her, they have already

Comment [U1]: Would be good to link to the section of the videocast here

been drained of financial resources, and are not capable of paying for testing. Dr. Lange also remarked on the lack of financial incentive for practices to provide for CFS patients.

Dr. Snell reminded the group that the primary purpose is to attempt to author recommendations over the next two days, and urged anyone to comment if they had relevant recommendations.

Dr. Dane Cook asked if functional neurological testing could be used to reliably support CFS claims, to which Dr. Lange immediately replied yes. Dr. Cook further asked whether the testing of impaired complex information processing could be simplified for wider usage, without requiring such an exhaustive battery of tests, and finally asked whether functional neuroimaging has a future as a test for CFS. Dr. Lange said that if funding were available to distill the testing such that it isolated what tests in isolation produced good psychometric data, this would be valuable. More research would be required to do this. She believes the functional neuroimaging data on a patient is best used as supportive evidence.

Dr. Nancy Klimas wondered whether one recommendation could be to have an education and certification program networked such that those who required assessment for disability would have a resource to consult with before being assessed improperly and forced to go through the appeal process.

Dr. Klimas stated that the SSA adjudicators have impressed her in general, and she believes they try to do a fair job.

Dr. Klimas remarked that they use an abbreviated Cambridge Neuropsychological Test Automated Battery (CANTAB) of only 45 minutes in length with some success, and echoed Dr. Cook's enquiry regarding using a more practical, short testing battery in disability assessment. Dr. Lange said that in private practice she uses the shorter Gordon Diagnostic System in children with some success, and is trying to publish a paper using a far shorter task than current batteries, however all this testing currently still needs to be properly put into context with other testing data and overall intellectual function.

With regard to the education and networking question, Dr. Lange pointed to the old CFS centers, and the VA centers of excellence as a good model. The Veterans Health Administration (VA) centers of excellence – one of which she heads in New Jersey -- involve a healthy synergy of clinical practice and research and develop the communication tools to facilitate this. She believes similar centers need to be implemented in one local area, rather than “pulling in” people from all over the country.

Mr. Steven Krafchick commented that in his experience as an attorney, an unknowledgeable neuropsychologist will often miss things in the same data that someone else finds quite fruitful. He believes that a curriculum, perhaps web-based, for medical schools and current neuropsychologists would be a good recommendation so they would know what to look for in testing.

Dr. Snell clarified that any unofficial recommendations would be compiled and voted on tomorrow.

Dr. Susan Levine wanted to know, given the prohibitive cost for many patients, whether a clinician could document impairments in speed of processing, and wondered whether there was a clinic to do this. Dr. Lange replied that there was no such clinic. Dr. Lange remarked that in terms of evaluating the speed of information processing and intellectual function as a clinician, either the Gordon (The Gordon Diagnostic System) or Conners' Continuous Performance Test (CPT) are available and they coincide with more rigorous testing. Dr. Lange prefers the Gordon for its ease of use. Dr. Snell says he uses a reaction based test which is computerized.

Dr. Arthur Hartz wondered how a patient with no money is to get an evaluation. Dr. Lange believes that this would require more qualified people to be trained, and hubs to train these people that could also serve as clinics. In response to how these could be funded, Dr. Lange suggests that her experience is with federal funding through the VA.

Dr. Jason remarked that the need for centers of excellence, for a variety of different needs has been recommended again and again, to no avail. He wonders whether their terminology needs to be changed, perhaps they'd be better served reframing these as networks of individuals arranged in hubs, but regardless he believes that this should be their top priority, commitment, and central recommendation. This suggestion drew applause. Dr. Snell agreed.

Mr. Krafchick reiterated the prohibitive expense of the testing, and promoted a more streamlined, directed battery would be cheaper and useful and could draw in additional funding. Dr. Lange agreed that this would be ideal but further research is required with CFS as the centrally determined research question, as many of the other tests drew from other research questions, and were designed around other patient populations.

Dr. Ronald Glaser recounted how a Doctor at the forefront of mind-body research had, 10 years ago, canvassed support from research-friendly senators to set up something similar to the recommended centers of excellence. A program was established for five centers, the one Dr. Glaser was involved with was on stress and wound healing. This was something that worked and should be looked at as a model for future success. He suggested that governmental figures could be contacted for support. Dr. Lange agreed citing similar types of success with the VA with gulf war sickness.

Dr. Marshall asked whether the cognitive dysfunction was unique to CFS. Dr. Lange replied this was not the case. Dr. Marshall remarked that the validation of any new more cost-effective screening procedure would be subject to the rigorous normal scientific process of disproving the null hypothesis. He believes there are two potentially conflicting goals: first that the test can make a diagnosis and monitor progress in therapy, second addressing the economic reality surrounding disability assessment. For example, more exhaustive and expensive testing would not be funded if someone was found not to have CFS by a cheaper more fundable alternative, so care is required.

Dr. Lange remarked that if testing meant that patient's cognitive function improved, this wouldn't necessarily mean they could function in the same way. Dr. Marshall indicated this would fall under SSA retraining etc.

Dr. Klimas wanted to stress that patients are very motivated to return to work in general, and many patients she's had experience with have been retrained and moved to other, more flexible work and been quite productive. She remarked that this aspect of Social Security hasn't proved problematic. She stressed that Social Security puts you below the poverty line and provides a massive incentive to work, and that any efforts at retraining and rehabilitation could only help the patient, regardless of the technical classifications and disability assessment.

PUBLIC COMMENT

The following section highlights key points made by witnesses who testified during the public comment session. Access to the complete text of witnesses' written testimony is available at: <http://www.hhs.gov/advcomcfs/meetings/presentations/10122010.html>

Dr. Fred Friedberg

- President of the International Association for Chronic Fatigue Syndrome (IACFS).
- Noted that CDC issued a job announcement for chief of their Chronic Viral Diseases Branch. This position would be responsible for the most significant US budget on CFS research.
- Expressed strong dissatisfaction with the attitude of the Chronic Viral Diseases Branch toward the scientific community surrounding CFS, which has created "mistrust and skepticism."
- Advocated on behalf of IACFS for a new chief who has the experience that would lead to a more open approach to the scientific community, especially those involved in retro virology, and molecular medicine. The new chief should be open to external input, and more transparent.
- Recommended new chief should post a statement of intent which would include their planned and current CFS research. The CFS program should have regular meetings to begin to adhere to the 5 year plan.
- Noted that this new approach he outlined would bring the chief more in line with the CDC's own mission statement.

Dr. Joan Grobstein

- Expressed frustration at the failure of the CDC to react to the Committee's revenue-neutral recommendation last October to reject the empirical definition of CFS, indeed they produced three studies using this definition. One of these

studies on XMRV used this empirical definition and was misleading and was harmful to patients.

- Remarked that doctors must act sometimes without knowing the exact cause of illnesses. Patients suffering with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) are denied any action as no testing is recommended. Even though our knowledge isn't complete, we can still treat patients.
- Stated that clinical trials should begin soon, and patients do not want to wait to be treated. It is unethical to withhold treatment on the known infections that ME/CFS sufferers have. There is science behind ME/CFS, just no funding, even from the ARRA (American Recovery and Reinvestment Act).

Lori Busby

- Remarked that there has to be a uniform way to subgroup CFS. CFS studies on human leukocyte antigens (HLA) must be described in a better way to subgroup patients in the future, as these subgroups may be a cause for the inconsistent results of HLA research thus far.
- Suggested one subgroup should be those patients with an infectious trigger who carry the HLA associated with diminished immune response.
- Stated that certain CFS patients may be genetically predisposed to a diminished immune response and statistically seem to have larger incidence of other issues. The fact that these other issues disqualify them for studies may be inadvertently skewing data toward patients with other causes for CFS which are non HLA related, and overrepresented depression as a feature.
- Suggested there could also be gender-specific differences, which should also be sub-grouped.
- Noted that one ground for this sub grouping could be by cataloguing at the blood bank.
- Thanked the practitioners and researchers who have helped her, in the context of so much medical prejudice against the diagnosis.

Thomas Hennessy Jr. (via phone)

- Welcomed the committee, attendees and members of the public, and thanked them for making the proceeding publicly accessible on the web.
- Described the total lack of confidence for decades on the part of most CFS sufferers, and the lack of action on the part of Health and Human Services (HHS) to respond to any recommendations made by the committee.

- Described the incomprehensible physical and mental “misery” experienced by sufferers.
- Recounted how he made a statement in 1989 at the first CFS meeting which proved predictive when arguing a new definition and name was required for CFS. He said if they didn’t get rid of the “F” word, “fatigue,” they’d condemn untold millions of sick people all over the planet to decades of misery and premature death. The disease has nothing to do with fatigue.
- Described the government and medical establishment as “heartless” and their response as a “medical crime.”
- Remarked that CFS sufferers want to go back to work, and are not malingerers.

Meghan Shannon

- Expressed gratitude to Dr. Jason and others gathered.
- Has a diagnosis of immune deficiency, also has post polio syndrome.
- Recommended that CFS should be part of any efforts to train and educate health providers under the health reform, by creating a website under the reputable HHS “brand”, which focuses on medically unexplained symptoms, and is a compendium of currently available research.
- Recommended designing an epidemiology study on prevalence and incidence of CFS in the US, which would include gathering the health status on household contacts. This may support her belief that the disease is contagious. The blood supply needs to be protected, as it is in the UK.

Nancy McGrory Richardson

- Education and Outreach Director for Hemispherx Biopharma.
- Described how Hemispherx Biopharmas conducted a study on XMRV monitoring a population of those with CFS diagnosis, which will be presented soon. They are moving forward with their work, looking toward FDA approval of Ampligen.
- Remarked that Hemispherx will keep the community informed of new sites they develop, and looked forward to working with the recruitment of new patients.

Dr. Jones indicated that in David Adonailo’s absence, Marly Silverman will be reading his statement.

Marly Silverman (reading David T. Adonailo’s comments)

- Founder of the Patient Alliance for Neuroendocrine-immune Disorders Organization for Research and Advocacy (PANDORA).
- PANDORA urged follow through on committee recommendations for five centers of excellence. New Jersey has passed a state resolution supporting this. Suggested there may be opportunities for success on the state level.
- Touted support for PANDORA in a recent Chase Morgan charity contest.
- Described conundrum where funding is required to delimit what research should be pursued, but funding is currently denied because that certainty on lines of inquiry doesn't exist. The new studies on the existence of MLV in CFS patients should provide an opportunity.
- Urged closing the funding gap between CFS and other diseases.
- Echoed other calls for centers for clinical training or primary care physician training on the proper diagnosis and treatment of CFS, and the adoption of diagnostic CFS criteria.

Denise Lopez-Majano

- Commented that she is not a patient, but her two sons are.
- Suggested that at least one month's notice should be given regarding scheduled meetings, to make travel arrangements, prepare statements etc.
- Requested more attention on quality of life. Gave account of her two children, suffering with CFS, concerning their day to day issues with functioning.
- Listed the various accommodations she makes for her sons, for comfort, sound levels, sleeping, physical therapy, following conversations.
- Asked the committee to help them get back the lives they deserve.

Cort Johnson

- Remarked that the NIH is capable but unwilling to help CFS. Many diseases get substantial increases in funding, even in hard economic times. They deserve to know why CFS gets no significant funding, and indeed has endured a historic decline under the charge of the Trans-NIH working group, including closing the three CFS research centers.
- Stated Trans-NIH working group must be put to task for not providing any sums of money for a reasonable request; that actions by way of funding should match their supportive rhetoric.

Dr. Jones thanked members of the public for all the comments given, and urged that everyone return promptly for resumption of the meeting at 1:00pm.

Dr. Snell clarified that the topics for conversation after lunch are not physical therapy and vocational therapy but functional capacity evaluation, vocational evaluation, and metabolic evaluation.

SUBCOMMITTEE LUNCH

FUNCTIONAL CAPACITY EVALUATION

Mr. Steve Krafchick introduced Dr. Ted Becker, who works in the capacity of a Physical Capacity Evaluator to the advisory committee. He conducts aerobic evaluations.

*Theodore J. Becker, PhD, RPT, CET, CEAS, CDE, CDA, CCI, FACFEI, DABDA
Physical Capacity Evaluator*

- Stated that overall goal today is to understand the scientific principles of work physiology regarding fatigue.
- Described fatigue as a warning signal, which if not heeded compounds recuperation time.
- Explained how physiological fatigue can be evaluated by heart rate recovery curves.
- Illustrated how Functional Capacity Evaluation (FCE) surrounding eight hour work has come under criticism. Some criticism has to do with the failure to discriminate between exercise and work physiology.
- Asserted work physiology does have a scientific foundation, and is a reliable and effective method for predicting full-time work. Work physiology has definite criteria for finding fatigue. There are numerous studies involving oxygen consumption, heart rate and heart rate responses to work, which can determine sustainability of work.
- Abnormal physiological responses to work involve the biomechanical aspect of the work reaching a steady state, but the heart rate not reaching a sustainable steady state. This is accepted as deconditioning.
- Illustrated how in extreme cases, even if the work is decreasing over time, there is no recovery. In a two day test their second day shows a marked increase in heart rate and recovery time.
- Noted that in his preliminary survey most FCE providers do not use accepted capacity testing protocol and formula, have inconsistent data, subjective and estimated evaluations, and incorrect methodology. Indeed, much of it is “made up.” The scientific foundation is there for predicting fatigue, it just isn’t utilized.

- Stated that these failures are detrimental to patients.

Dr. Klimas asked if a person has a sedentary job, why would their heart rate matter? Dr. Becker said that there needs to be an understanding that sedentary work requires sustainable posture and positioning as well as upward extremity and/or other muscle function. There is energy consumption in what appears to be sedentary work, and for those with systemic dysfunction, even this modest exposure can produce the extreme compounding fatigue outlined previously. He pointed to federal regulations on exposure to seated jobs like truck driving, flying planes due to fatigue concerns.

VOCATIONAL EVALUATION

Mr. Steve Krafchick introduced Kathy Reid, a vocational and rehabilitation counselor he worked with previously in interpreting the medical records, neuropsychological testing, and physical capacity evaluations to determine whether someone was capable of work.

Kathryn Reid, MA, CRC, CCM, Rehabilitation Counselor

- Described her work as translating or segueing between the technical information and Physical Capacity Evaluation (PCE) Report to their application to a particular individual and their job.
- Provided background on vocation rehabilitation and how it is applied in different settings. The history goes back to benefits for veterans coming back from wars with amputations and a wide variety of injuries and disabilities. Federal legislation continues adding benefits and protecting individuals with disabilities from discrimination.
- Described how Earning Capacity Assessment is done, how policies vary in how long they provide for pre injury levels of earnings, and involve many exclusions for mental health conditions.
- Stated that denials for CFS are based on a mental condition being primary, or discounting of documentation due to subjective testing.
- Stated these denials are compounded because many in-house company vocational counselors make errors and are not exhaustive.
- Stated that PCE's are also very shaky on denied claims, often aren't very specific to the worker, and under review often require amendment of extended statements from physicians to fill in the holes of the documentation.
- Remarked that Social Security does look at the ability to perform a full work week in terms of their work behavior. However this analysis is often quite primitive and doesn't analyze the nature of the job. Sometimes it involves looking at absences without context.

- Describes how employers will often provide sick time, but take disciplinary action in response to absences which defeats the purpose, and makes things impossible for those with CFS.
- Described how DOT's classifications of level of work are very limited and do not involve posture in a meaningful way, which is problematic for CFS and other illnesses.
- Clarified that while PCE testing is useful, it should be put in context with a more developed understanding of what the person's work day is, what breaks they have, what posture they have, how much they have to walk etc. This context provides a far more substantial report for insurance reviews, and is developed on objective data.
- Provided case examples where review was overturned due to a mischaracterized level of work and one where PCE data were not objective.

METABOLIC EVALUATION

Dr. Snell

- Credited Dr. Staci Stevens, the executive director of the fatigue lab at the University of Pacific.
- Summarized the history this Cardio Pulmonary Exercise Testing (CPET) knowledge being modified for measuring CFS and disability assessment.
- Agreed with much of Dr. Becker's opinion on functional capacity evaluation not doing what it is supposed to do, and indeed undermining CFS patients.
- Stated CPET can determine impairment and function objectively using a number of different measures:
 - Peak Oxygen Consumption (VO₂) max
 - Anaerobic Threshold
 - Heart Rate
 - Blood Pressure
 - Ventilation
 - Describes CPET as a widely accepted "Gold Standard" of measuring functional capacity, and supports this with quotes from various different organizations, including the SSA.
- Noted that when used to evaluate respiratory, circular and other functional aerobic impairments, reports are held to a lower standard than when used to support CFS.
- Described how, upon following up on initial classification of severity of impairment tests, they found CFS patients were unusually disabled and had far longer, completely abnormal (longer than a week) recovery time. This drew them to investigate post-exertional malaise.

- This data fits the general pattern of many CFS symptoms being delayed.
- Described how they adopted a test-retest strategy they call the Stevens' Protocol, over two days, other than in cases of severe impairment. The second day of testing shows significant limitation among CFS patients compared to control, across a range of different testing methods. The testing is enough to predict CFS with accuracy.
- Defended the validity of this test against routine questions of obesity, effort, and reconditioning.
- Emphasized they all know this is political, as well as scientific and medical. CFS, though similar in some ways to overtraining Syndrome, is looked at far more skeptically.

Dr. Levine wondered whether, due to patient fears of relapse due to exhaustive testing, a lighter test could be performed. Dr. Snell indicated that this was not possible, the standards were more rigorous for CFS because there are often questions of effort, and these results would not hold up. He also indicated there is extensive monitoring for safety purposes, and they require physician referral. Mr. Krafchick added that there is a risk stratification form which screens out those who aren't suitable.

Dr. Glaser wondered whether these tests had been used to evaluate anti Epstein Barr Virus (EBV) drugs. Dr. Snell indicated they had been involved in a study that had looked at that, but would like to run the tests in his own lab and thought it would be a good method for any clinical trial.

Dr. Klimas wondered about the before and after assessments on cognitive functions. Dr. Snell said they did do a reaction time cognitive test and consistently they found CFS patients with reaction time cognitive deficits on the second day of testing. Dr. Klimas wondered how long the tests were, and Dr. Glaser indicated 8-15 minutes at maximal effort.

Dr. Hartz asked how these tests correlate to subjective measures of their symptoms, and Dr. Snell indicate they correlate very well, and support a diagnosis of CFS. As to Dr. Hartz's question regarding whether it could measure severity, Dr. Snell said they could say one person was sicker than another, but is not sure how it would relate to other measures. Dr. Hartz wondered whether they saw different levels of effort on the second test, but Dr. Snell clarified that the test was not begun until those objective criteria for effort had been met.

SSA PRESENTATION ON IMPROVING DISABILITY ASSESSMENT PROCESS

Dr. Jones introduced Mr. Mike O'Connor, the SSA ex-officio representative to CFSAC. SSA and HHS parted ways years ago, but SSA has been involved in response to CFS from

the beginning. Dr. Jones lauded his responsiveness as a subcommittee member. He will be presenting SSA's progress in improving the disability assessment process.

Mr. O'Connor, Social Security Administration, Office of Disability Programs

- Stated that the SSA has taken an active role in acknowledging the potentially disabling consequences of CFS.
- Listed the various improvements SSA has made by updating guidelines and instructions to adjudicators on assessment of CFS. These guidelines emphasize the need for careful documentation and evaluation especially of cognitive deficiency.
- Discussed how guidelines indicate that symptoms of CFS may cause limitations beyond what objective tests demonstrate, and that someone can be judged to be disabled based on symptoms, if supported. SSA requires objective data to make some determination resulting from signs, symptoms and laboratory findings, not just description of symptoms.
- Remarked how, to allow for medically determinable impairment, medical signs and laboratory signs for CFS were itemized in a SSA ruling, however others can be used if it's accepted medical practice. Additional signs can be discovered, and they will look to amend this ruling.
- Referenced publication for healthcare professionals which provides guidelines on assessment of CFS patients. This is available on www.socialsecurity.gov
- Highlighted SSA commitment to CFS education:
 - They continue to conduct periodic training as part of an ongoing effort to ensure that all adjudicators and doctors are informed about CFS and understand how to evaluate it.
 - Every new adjudicator and doctor is trained on the evaluation of CFS.
 - They include a chapter on CFS in the training manuals for new disability adjudicators, doctors, and administrative law judges.
 - Quality assurance program provides feedback on cases.
 - Stated that these measures show a long-term commitment to assist individuals who are disabled because of CFS.

Dr. Jason stated the committee had prepared a list of questions and sent them to the SSA a year and a half ago. He wondered whether the SSA received them and knew the types of issues that were of concern, especially complaints about differential treatment? Mr. O'Connor is familiar with the request and did provide some data last year in response to that request. Dr. Jason expressed that rather than a basic history of the SSA's involvement with CFS, it would prove more useful to have responses to these questions of treatment.

Dr. Jason asked Mr. O'Connor why CPET was not on the list of objective guidelines. Mr. O'Connor responded to the question on exercise treadmill testing by saying that while

it's not on the list, they consider all medical evidence from a person, if it is part of their medical record. Dr. Snell and Mr. Krafchick both indicated that while CPET testing isn't explicitly on the list, it is accepted as evidence of a diagnosis by SSA.

Mr. Krafchick wondered how they could improve, or inform about the rulings of recidivist adjudicators. Mr. O'Connor said you can contact the state agency for disability claims, but everyone has the same national curriculum for all disability adjudications and administrative law judges.

Dr. Hartz said that given that symptoms alone were not adequate for determining disability for the SSA, and the science may not have caught up in terms of testing in that local area, that it was a very high burden of proof. Mr. O'Connor stated it was a matter of their law, and they must establish, as with any impairment, objective medical evidence, but their guidelines specific to CFS helped to address this.

Dr. Klimas followed up on Dr. Jason's inquiry about the prepared list of questions they had formerly sent and said that they had wanted more transparent data broken down regionally to determine how many CFS patients were refused disability on the first level of an appeal, and whether there were regional or other inequities across the system. They had been told there was no ability to search for this data. Mr. O'Connor said he would follow-up on the requested information.

Dr. Klimas requested that CFSAC receive the chapter of training material he had referenced. Mr. O'Connor stated that the SSA rulings are designed to be open-ended to new medical developments.

Dr. Michael Houghton wondered how many criteria have to be met to be labeled a disability, such as the antibody titers. Mr. O'Connor stated they are just examples that were given as an objective measure of a person's illness, that only one might be necessary.

Dr. Levine asked if it would be sufficient to have the laboratory data rule out other illnesses; a diagnosis by elimination. Would that be considered enough objective evidence? Mr. O'Connor said they would need positive objective evidence in the form of signs or laboratory findings.

Dr. Snell wondered whether the SSA takes activities in daily life into account, in addition to the capacity to do a job when they make these evaluations, i.e. they can "do the job, they just can't get there." Mr. O'Connor said the SSA instructs the adjudicators to obtain the activities of daily living from the claimant and third parties, including guidelines on sustainability.

Dr. Jason asked Mr. O'Connor, given the speed of development in the field, if there were any opportunities to work with him or his office to think about some of the new developments and how they might be introduced into materials, guidelines, or other types of regulations that he is involved in. Mr. O'Connor said that they are always open to information, that's why they are involved in CFSAC.

Dr. Jason wondered what the process was for making the updates to ruling. If information is given, at what point do they make changes? Since issued in 1999, the SSA ruling has not been updated, wouldn't it be relevant to reevaluate it after 10 years?

Mr. O'Connor said that they are looking at updating the ruling, and the updating process involves looking at current research to see what has been suggested as additional diagnostic criteria. There is no public comment mechanism for rulings, only for regulations, but they would be willing to work with outside advocacy groups. He was asked if SSA would be willing to share a draft of the rulings so the committee could comment. Mr. O'Connor stated that is a possibility. Dr. Jason said that this would be something of great interest to CFSAC and urged Mr. O'Connor to bring the suggestion to his superiors.

DOL/ERISA PRESENTATION

Dr. Jones welcomed Elena Lynette, who is presenting on other benefit programs underneath the Department of Labor's Employee Retirement Income Security Act (ERISA).

Elena Lynette, Senior Health Law Specialist, Employee Benefits Security Administration's Office of Health Plan Standards and Compliance Assistance, Department of Labor

- Introduced herself as well her colleague, Kevin Horahan
- Stated that aspects of ERISA might relate to those with CFS. The law was originally to deal with employee based pension plans, but it has been expanded significantly within part 7 of ERISA dealing with group health plans under the Consolidated Omnibus Budget Reconciliation Act (COBRA), as well as the Health Information Privacy Act (HIPAA).
- Detailed the aspects that most relate to CFS as follows:
 - Those with CFS who cannot work can extend coverage under COBRA, at significant expense.
 - HIPAA affords a special enrollment opportunity to go under a spouse or if they are a dependent, their parents' plan.
 - HIPAA portability rules also mean that if they had creditable coverage, they could avoid preexisting condition exclusion when moving to a group health plan upon rejoining the workforce.
 - Prohibition of a health insurance issuer denying someone based on a health factor, or charge a higher premium.
 - Mental health parity laws, which came in two waves:
 - Parity in dollar limits for mental health limits was required
 - Benefits for medical surgical now needs to be equal to mental health in non quantitative treatment limitations as well, for instance the process for deciding what is covered.

- Additional changes are dictated by the ACA which will be discussed later.
- Encouraged people to access www.dol.gov/ebsa
- Stated that they have lots of publications and informal guidance in addition to their regulations that are published on a continual basis, copies can be made available.

Dr. Jones noted that the CFSAC website would link the Labor website for the brochures and publications.

In response to Mr. Krafchick, Ms. Lynette clarified her group does not do ERISA disability regulations. She said she would get a contact for that group for a future conversation.

Mr. Krafchick revealed that the disability benefits are not adhered to or interpreted correctly by courts, and that this is a prime issue. Mr. Krafchick wondered what department in the Department of Labor was in charge of that. Mr. Horahan said it would be within their agency, just not their particular office, and reiterated they could get them in touch with them.

Dr. Jason wondered whether they had any issues come up with ME/CFS, and asked who within the agency would be appropriate to contact. Ms. Lynette indicated herself and Mr. Horahan were a good initial point of contact, and that she had no personal experience regarding ME/CFS issues, but many times they didn't get into the detail of the actual condition, so this was not surprising.

Mr. Krafchick commented that the ERISA Disability Plan specifically limits coverage for both fibromyalgia and CFS. Mr. Horahan said that because disability plans aren't considered group health plans they aren't subject to the rules itemized by ERISA part 7.

Dr. Klimas commented that many patients have to use COBRA while they wait for SSA to be processed, which takes many years due to initial rejection. The financial burden of this is severe, and they generally lose their house. Dr. Klimas wonders how these disparate governmental agencies can come together to get things working. Mr. Horahan said there may be some relief in coming years through the ACA. Ms. Lynette expressed sympathy and said they experience many of the same issues.

Dr. Jason asked whether there are ever times within Ms. Lynette's agency where there is such a crisis that occurs such that a special task force is put together to look at the unique needs of an individual? Ms. Lynette is not sure if they have ever looked at a disease-specific issue, but rather the focus is more on displaced workers, and there isn't an official mechanism in place for this. There are occasional instances where an individual may come up in an extreme situation, but it isn't a formal taskforce. Mr. Krafchick remarks that if a denial of coverage would result in death in an ERISA plan, there is no remedy for the injured people.

Ms. Lynette says feedback is welcome, especially on recently published work, and these suggestions will be forwarded to the relevant people.

Dr. Snell asked whether the COBRA data is coded by illness? Mr. Horahan mentioned there isn't really any good COBRA data.

Dr. Jason returned to the previous conversation about crisis/life-threatening situations, and stressed that it needs to be understood that this "is a class of people with very severe health problems who oftentimes have not been properly attended to by the health care system."

HEALTH CARE REFORM – IMPACT ON PERSONS WITH CFS

Dr. Jones introduced Mayra Alvarez, who will be presenting information on the ACA.

Mayra Alvarez, MHA, Director of Public Health Policy, U.S. Department of Health and Human Services, Office of Health Reform

- Stated her focus will be on the implementation of the ACA.
- Expressed excitement about the ACA. Thanks to health care reform, all Americans will be able to get the health care coverage they need. Touts the following elements:
 - Incentives for small business
 - Closing the prescription drug donut hole
 - Relief for those with preexisting conditions in the Preexisting Condition Insurance Plan
 - The early retirement reinsurance program to provide relief for employers and enable early retirees to get quality affordable care
 - Dependents can stay on their parents plan until age 26
 - Ending the worst insurance company abuses, including:
 - Denials for preexisting conditions
 - Denials for unintentional mistakes on applications
 - Life time limits on coverage, and annual limits
 - Restricting which doctors you could use
 - Restricting which ERs you can use
 - Lack of third party oversight or appeal on coverage decisions
 - Cost sharing requirements on preventative services
- Stated the Act looks at health care as a whole, not just insurance reform. For instance, they are creating new state based insurance exchanges, expanding Medicaid, expanding the prevention and public health focus for the healthcare system by promoting local level initiatives on wellness, for instance on obesity and tobacco cessation.
- Encouraged people to visit www.healthcare.gov and touted its user friendly approach which includes tools to compare insurance plans.

COMMITTEE DISCUSSION

Dr. Jones mentioned that one national insurer does would not cover doctor visits regarding CFS. How does the ACA change this? If you could now get coverage due to preexisting condition protection, how do you know whether you will still be covered? Is there a process of appeal?

Ms. Alvarez stated the ACA does provide consumers with the additional tools to appeal insurance company decisions. Not only through an internal appeals process, which most insurance companies have today, but also through a third-party independent entity that will be established at a state level. Also, Americans should be able to choose which insurance company they want based on their needs. The website helps achieve this, much like a search aggregator like kayak helps people buy plane tickets.

Mr. Krafchick wondered if her group was going to keep track of the prices insurance companies are charging. Ms. Alvarez stated yes, that while insurance regulation will be left to each state, there is some oversight on rate increases which aren't seen as justified. Mr. Krafchick understood that in the ACA there could not be a limit on treatment for any specific medical conditions. Ms. Alvarez confirmed this and indicated that they are studying the minimum level of coverage the ACA will impose in 2014. Whether they will look at specific diseases is part of the ongoing discussion.

Dr. Jason wanted to know Ms. Alvarez's personal reaction to the national insurer's denial of doctor's visits on CFS, and whether discussions surrounding implementation of ACA could involve the CFS individuals cast out of the system and denied healthcare because of discriminatory practices, and lack of available care? Ms. Alvarez's personal reaction is she doesn't think any person should ever have to struggle with finding medical care or finding a doctor that's willing to take them, regardless of the disease they have, the color of their skin, or their level of income. There are many challenges surrounding implementation, and changes will surely be made. The more they are committed to working together and engaging in dialogue that answers questions and meets needs, the better they will be.

Dr. Jason asked if it's possible to have dialogue regarding the fact that there are still populations being discriminated against. Ms. Alvarez concedes there are going to be populations left out, and the law isn't perfect. Investments in Community Health Centers will strengthen key safety nets which will provide some relief.

Dr. Jones clarified that many of the regulations implementing the ACA are being written with Centers for Medicare & Medicaid Services (CMS) in the lead because they are the health insurance component of the department. Dr. Jones asked if there is any way to access this rule making at the planning stage. Ms. Alvarez recommended the general HHS press list as a good resource to see new announcements.

Mr. Krafchick wanted to know if there could be access at an earlier stage. Ms. Alvarez said that the fact that the committee had members in CMS and the Agency for

Healthcare Research and Quality (AHRQ) suggested they would have an avenue for input.

Dr. Levine asked if the ACA has made any provisions for chronic illnesses, such as Gulf War Syndrome (GWS) or CFS. Ms. Alvarez said that they would have recourse in the third party appeal part of the ACA. She said that there is a huge effort around chronic disease in the ACA, regarding better coordination of care across the departments.

Dr. Marshall said that recommendations formulated must be pragmatic to move them forward. There have been years of recommendations put forward which are not adopted, and then are characterized as being ignored. Though some things require money, and should not be forgotten, there are some budget-neutral recommendations that are more actionable.

Dr. Snell said that the system will often frustrate even these budget-neutral recommendations. The system isn't a complete hierarchy, they need to get people at lower levels to be invested in dealing with these recommendations, and adopt them. Dr. Jones agreed that it isn't a situation where directives are issued from the top down, but that there are also many occasions where groundswells at lower levels move upward.

Dr. Snell said a good example would be revising the guidelines on CFS at the SSA, as a result of having the right people at the meeting.

Eileen Holderman agreed with Dr. Marshall. It is the small, no-cost things that seem to be no-brainers where they can make headway, but she doesn't want to back away from being bold and asking for real funding for this disease. Many patients are asking for funding for research, not just treatment, despite the severity of their condition, and given the cost of treating the disease, money is required, even in a recession.

Dr. Klimas stated the *ex officio* members have been very informative, but wondered whether when they leave they consider themselves a task force? Dr. Jones indicated they do a monthly conference call in order to network, the commitment is there, and they are responsive. Dr. Miller said that he found the calls very helpful.

Dr. Jason said that he found the open times for discussion in the meeting were helpful, especially after presentations. He mentioned there is more receptivity for significant changes, and a chance to "do something historic," if the recommendations were focused and bold.

Eileen Holderman followed up and said that recent research had made for a more receptive environment. She argues there are sound economic reasons to ask for funds as well. Dr. Klimas said research would pay for itself if only 100 people were put back to work.

PUBLIC COMMENT

The following section highlights key points made by witnesses who testified during the public comment session. Access to the complete text of witnesses' written testimony is available at: <http://www.hhs.gov/advcomcfs/meetings/presentations/10122010.html>

Robert Miller

- Introduced himself as 25-year CFS patient.
- Requested more input from the *ex officio* members.
- Read message to the NIH Director, Dr. Francis Collins, and NIAID Director Dr. Anthony Fauci asking what they have done for ME/CFS, and what their response is to the hundreds of emails they have received over the last week.
- Reported on a meeting prior to the recent XMRV conference, where he presented two petitions regarding the CDC being allowed to publish on its inability to find XMRV before the NIH/Food and Drug Administration (FDA) study confirming MRV's in CFS patients was released.
- Remarked on the lack of trust felt toward the NIH, \$100 Million should be earmarked for CFS, and they should establish expedited funding and research process, just like what was done with AIDS.
- Advocated for funding required for the centers of excellence which have been proposed year after year.
- Stated that the NIH and FDA have paralyzed drug development, which has led to self-administered treatment, and encouraged the FDA to stop blocking Ampligen which has helped him.
- Said patients are demanding that the Secretary of Health honor the committee's hard work and honor the decades of suffering of CFS patients by replying to the CFSAC recommendations with concrete answers, and said it's time to act on recent historic research findings.

Mike Dessin

- Agreed that the panel should follow-up with the SSA representative, as it seems the disability assessment process is quite outdated.
- Recommended the panel revisit the topic of changing the name CFS to its original name of myalgic encephalomyelitis. CFS is a demeaning name which makes many not take the disease seriously, and hurts the cause. In addition, they should identify other conditions in the CFS spectrum and properly name those as well.

- The disease is severe, reduces life span, and can even prove fatal.
- Suggested the committee read a paper by Pat Fero: “Inadequate NIH funding for CFS” which demonstrates the ever diminishing funding for the disease.
- Expressed frustration with lack of access to competent care for patients, and a lack of insurance coverage for care.

Mary Schweitzer

- Updated everyone on her medical condition, citing the use of Ampligen as helpful.
- Commented on the issue of insurance testing. Cigna made her go through occupational testing in September of 2001. On the second day of testing she passed out, but it was reported that she refused to continue testing.
- Echoed the several other calls for the name of the disease being counterproductive.
- Asserted that competing international definitions mean that patient populations are not matched, as some involve significant overlap with psychiatric conditions. There are multiple different CFS definitions, and it has become more of a mutable social construct than a scientific definition.
- Suggested the most pertinent question regarding XMRV is not whether they cause CFS per se, but rather does XMRV have an impact on the people with the disease. Urged that careful attention should be paid to cluster outbreaks.
- Requested the committee go back to the research published in the 1990s and 2000s in peer-reviewed journals, which were starved due to lack of funds.
- Stated that while each individual bio marker or disease surrounding CFS doesn't directly cause the disease, and not everyone with the disease has each one, this shouldn't be cause to reject them; the disease should be looked at as a whole.

Marly Silverman

- Introduced herself as the Founder of PANDORA.
- Described the struggle CFS/ME patients have dealing with ERISA disability insurance, and the difference between the theory and practice of insurance.
- Claimed the burden placed on the patient to prove their diagnosis is extreme, particularly at a vulnerable time, and asserted it relies on the assessment of those who have never seen the patient, and not their treating doctor.
- Described how the struggle with CFS drains patients of all wealth and condemns them to a low quality of life.

- Expressed anger with how insurance companies deny until the employee gives up, or makes a legal error when navigating their convoluted legalese.
- Described a pattern of harassment from insurance companies.
- Suggested to ERISA that insurance companies should not take away access to Medicare until the ACA takes place.
- Echoed the various calls for NIH to increase funding.

Carol Geraci (via phone)

- Stated the CDC's refusal to investigate CFS for 30 years is “morally wrong, deeply disturbing, appalling, and outrageous. These are serious crimes against human rights violations, medical misconduct, malpractice, premeditated genocide, government fraud, crimes against humanity and discrimination.”
- Claimed the CDC should be held criminally liable for making a faulty definition for people who are gravely ill. They should be held criminally liable for allowing people to suffer and die, and ignoring publications and research scientists that have been warning the CDC that patients have been suffering severe immune and neurological problems for 30 years.
- Asserted that ignoring the disease could cause an AIDS-like epidemic.
- Encouraged patients of similar diseases; fibromyalgia, Gulf war syndrome and CFS should band together.
- ME/CFS continues to be called controversial, even though many diseases have unknown etiologies, and get clinical treatments, trials, and medication.
- Urged that Ampligen should be made available, and that those with limited means need access.
- Pleaded for redress of her suffering and sympathy for the suffering of those with CFS as a medical emergency, and read a plea from her sister for treatment.

Keith Baker (via phone)

- Described how, after being a successful student and excellent athlete, he fell victim to CFS which spread through his family. As he is adopted, he doesn't believe the explanation for so much of his immediate family having CFS is genetic.
- Stated that men underreport CFS, and it should not be portrayed as a female disorder or this will exacerbate the problem.

- Suggested there may be a connection between CFS and autism, as he has two children with autism, and many other CFS patients he knows also have it, and a study should be done on children of CFS patients.
- Questioned why CFS gets about the same funding from NIH as hay fever and other relatively minor diseases, receives no major research grants, and receives no federal funding.
- Expressed a lack of trust in the CDC's ability to conduct honest, unbiased research. Through the years, the CDC has abused ME/CFS patients in the following ways:
 - Naming the disease Chronic Fatigue Syndrome
 - Labeling the Lake Tahoe outbreak as hysteria.
 - Exposing personal bias by expressing that they expect to fail to validate XMRV connections
 - Making insinuations of contamination in studies.
- Defended the findings of promising XMRV studies and regrets the prejudice toward the disease.
- Urged the FDA to approve Ampligen, which he believes would also help legitimize the disease.
- Urged the government to ban CFS patients from giving blood.
- Requested higher level participation at the next meeting.

Pat Fero (via phone)

- Recounted a history of her study of NIH funding for CFS over the last decade.
- Submitted a final three page report on NIH funding based on Freedom of Information Act Requests, which shows a drop from 24 percent funding rates in 2000 to only 5 percent funding today. This report is not born out of a scientific or academic background, but she stands by her research.
- Urged CFSAC to begin an investigation of CFS NIH funding, which she will support.
- Queried the CDC's 2007 panel reports suggestion of acceleration of aging, and wants to know more about the data for this, see the proof, and know what early onset symptoms are.
- Questioned how the CDC proposes to study prevention when they can't define the problem. Suggested they check for markers in early onset diseases which normally affect the elderly.

Dr. Jason stated that Ms. Fero referred to a report, which is not in the handout materials. Dr. Jones announced they will make it available to the committee.

Susan Magowitz

- Recounted her personal history with a variety of conditions and diseases which led to CFS. She was ill for 15 years and has dealt with the disease symptomatically with the help of an array of different specialists.
- Detailed the suffering she has endured, especially early on with the disease.
- Credited the use of growth hormone, as well as her symptomatic treatment with the improvement of her condition, which was at a cost of \$25,000 per year.
- Described the limitations of her management of the disease, for instance she will spend days recovering after the exertion of coming to this meeting.
- Reiterated the calls for treatments, educated doctors, regional CFS centers, clinical trials for CFS treatments, and Ampligen and AIDS drugs approved for CFS usage.
- Stated funding is the primary necessity.
- She blames the CDC for wasting the lives of millions of CFS patients.

Dr. Jones thanked all participants for their contributions.

Dr. Snell previewed the following day's schedule.

ADJOURNMENT

The Chronic Fatigue Syndrome Advisory Committee was adjourned by Christopher Snell, PhD, on October 13, 2010.

THURSDAY, OCTOBER 14, 2010

CALL TO ORDER/OPENING REMARKS

Dr. Jones said she would do whatever possible to provide the video that was not web cast yesterday. She recognized the efforts of those in the advocacy community, however people in the background needed to be mindful of their movement because a few viewers had complained it made it difficult for them to focus on the speaker.

Acknowledged the efforts of the video cast and sound team for their efforts, the video from yesterday can already be viewed. Thanked those dealing with the considerable effort concerning logistics and travel.

ROLL CALL, HOUSEKEEPING

Dr. Jones conducted roll call with the following results:

Present: Dr. Christopher Snell, Dr. Dane Cook, Dr. Ronald Glaser, Dr. Arthur J Hartz, Ms. Eileen Holderman, Dr. Houghton, Dr. Leonard Jason, Mr. Steven Krafchick, Dr. Nancy Klimas, Dr. Gailen Marshall Jr., Dr. Susan Levine

Ex officio members present: Christine Williams, Dr. Michael Miller, Ms. Elaine Perry, Dr. Deborah Willis-Fillinger, Dr. Eleanor Hanna, Dr. Dennis F. Mangan (alternate)

Noted Dr. Marc W. Cavaille-Coll and Mr. Mike O'Connor will be arriving later.

Absent: Dr. Tracee Treadwell, Ms. Cheryl Williams

Linda Price was commended for her work.

Dr. Jason stated his concern that at this crucial time, where ex officio members are all the more relevant, there isn't enough time allotted for conversation with them. Dr. Snell says that they can move the ex officio discussion to the first item on the agenda, since there is much overlap with the science discussion anyway.

Dr. Snell officially opened the meeting.

Dr. Jones noted the two new *ex officio* members as a result of the recommendations of the previous meeting, and formally welcomed Christine Williams from AHRQ, as well as Ms. Perry representing the CMS. Stressed that because they were new, they would be listening more than speaking, but would be actively involved going forward.

AGENCY PROGRESS ON RECOMMENDATIONS

Dr. J. Michael Miller, Associate Director for Science, National Center for Zoonotic, Vector-borne, and Enteric Diseases

- Represents the CDC
- Stated that there have been significant changes to the CDC of late, with a new Director, and reorganization of many components.
- Stated this reorganization impacted the CFS program. Two centers were merged, forming the National Center for Emerging and Zoonotic Infectious Diseases.
- Described the uncertainty and difficulty surrounding this change, including moving location, losing many primary members. They are seeking a new branch chief.
- Detailed the selection process for the new branch chief, which they have little control over.
- Explained how they had continued in their work as much as possible, under the adept leadership of the acting branch chief, Dr. Elizabeth Unger, but had not taken on any new programs due to the leadership change.
- Stated they had recently clarified wording on disability on their website, and said they would incorporate some of the points raised in this meeting to take out inappropriate wording.
- Said they had made revisions to the ICD9 and ICD10 codes (International Classification of Diseases)
- Described the development of a new CME course.
- Listed the three major studies they are currently reviewing:
 - Registry of Unexplained Fatiguing Illnesses and Chronic Fatigue Syndrome, a pilot study with 141 patients

- A follow up study of Chronic Fatigue Syndrome and Chronic Unwellness in Georgia. Data has been cleaned for this and is being analyzed. This study will investigate the content validity of the various elements added to the 1994 case definition. This should prove instructive for a case definition consensus meeting that they are planning.
- The Pathophysiologic Mechanisms of CFS. This included neuroimaging, neuroendocrinology and genomic data. Data cleaning is almost complete.
- Announced that a new research data center has been formed which will allow for sharing of data sets. Data will start being available this year. Requests for data would go to the data center and not to individual offices.
- Described that the CDC has been engaged in XMRV activities, for CFS and national blood safety, but their CFS program does not test for XMRV or retroviruses in their laboratories; this is dealt with in a separate lab.
- Remarked he would like to see a standardized testing method agreed upon for XMRV before sinking resources in, so everyone was speaking the same language, but this would be dealt with by the Retrovirology Group.
- Referred to work on the prevalence of XMRV in blood donors looking at blood, organ, and other tissue safety groups.
- Stated that the CDC is always receptive to information from CFSAC.

COMMITTEE DISCUSSION

Dr. Snell welcomed Dr. Elizabeth Unger of the CDC from the audience and invited her participation. Dr. Miller gave a brief introduction for her and Dr. Kim Hummel, also from the CDC.

Dr. Jason expressed thanks for the sharing of data sets that Dr. Miller mentioned.

Wondered if they could state the implications of the science items presented on a previous day of the meeting on CDC policy, as well as standards. Do they feel the CDC has the same types of standards presented and whether the CDC is playing a leadership role? Also expressed agreement on the necessity of a case definition consensus meeting, but wondered whether they continue to use the Reeves 2005 criteria given new information? CFS and myalgic encephalomyelitis were not in the most recent drafts of the ICD 10 frameworks.

Dr. Unger said the talks on the science day [October 12] will be incorporated into the CDC's program, in particular the genomics elements were interesting. The heterogeneity of the illness was a particularly salient point. While they use a 1995 definition, they are not dogmatic about it; the chief focus is to give a "full dimension to the spectrum of illness" in those being studied. The Georgia surveillance study data is being used to compare different instruments, and they have incorporated many valid

concerns about their use. Argues that there is a need for viewing CFS with some dimensionality, rather than a single simple definition vs. control, which was a feature of the science day.

Dr. Unger clarified the ICD 9 and ICD 10 codes. There is a CFS code in the signs and symptoms chapter, and a different one in a different chapter for Post Infectious Fatigue.

Dr. Susan M. Levine inquired about the two different branches, the CFS Working Group and the Retrovirology Group. Is there a dialogue being established between the two groups? Are there samples from the Wichita group that are to be tested for XMRV? Dr. Miller said there have been biweekly face to face meetings between the different groups.

Dr. Unger said the Wichita samples were part of the first study and are significantly depleted and may not be enough for a new round of testing. One of their goals is to figure out the best way to make additional samples available for XMRV testing, but they must first determine the best way to do sample collection processing.

Dr. Dane B. Cook asked if there were any plans to make the neuroimaging data and the protocols used publicly available in their raw data form, so people can use the data differently, and work on standardizing protocols. Dr. Unger said that the data center is brand new, and doesn't usually deal with raw data. They will have to work out the best way to proceed, but are open to the idea. Dr. Jones, Dr. Unger, and Dr. Miller all remarked on the significant cost of making this data available.

Dr. Klimas suggested when considering the case definition, it would be worthwhile separating out exercise-induced patients. Dr. Unger said she definitely got this message from the science discussion.

Dr. Arthur J. Hartz asked Dr. Unger if she could speak to her philosophy, in regards to having a more politically-vulnerable broad definition, for research. Dr. Unger believes every study should make sure they characterize the dimensions of the illness in patients, not just a yes or no (for meeting criteria). The findings in CFS are not unique to the disease, but it's the constellation of those varying parts which makes the disease.

Dr. Hartz presses her for the rationale for doing it the way they do it now, rather than having a consensus definition which determines what patients are in a data set? Dr. Unger said it allowed for more flexibility, making for data which is more tailored to a subset of patients. Dr. Unger said both definitions have a place.

Dr. Hartz queried what the mechanisms are for incorporating new research findings into new inclusion criteria and how to analyze the data, such that they stay up to date. Dr. Unger said they are science-based and are peer-reviewed and stay abreast of current knowledge.

Dr. Marshall described how many physicians see psychosomatic illnesses in CFS patients and this causes suffering. The CDC has previously been thought to see the issue as more mental, or even not real, and not an infectious disease. Could she speak to the personal

dimension of the disease, and try to involve all aspects, including clinical and social aspects, of the disease in their investigation?

Dr. Unger said there has never been any doubt in the CDC of a biologic basis for CFS, but said referring to a disease as psychosomatic is not meant to infer that it is imagined or made up, but rather it was a reflection of the mind-body connection. CFS requires a multidimensional approach.

Dr. Eleanor Hanna wondered if the Research Data Center was part of the National Center for Health Statistics (NCHS). Dr. Miller said it was CDC-wide, it didn't belong to one center.

Eileen Holderman remarked on the apparent contradiction of using different definitions for study groups while encouraging standardization. Dr. Unger said many papers don't explain how they apply the 1994 case definition, which has many ambiguities. Instead, they spelled it out, and used instruments to determine what cut offs make the most sense. This will lead to more reproducible groupings of illnesses, with more dimensionality. Hopefully this will address some of the issues that have stymied progress.

Dr. Jason stated how focusing on a single biological marker, and dismissing it because it isn't found in all patients with a disease is problematic. This happened with a couple other diseases, where the more appropriate response might be to subtype, that the marker is important but not essential. With this as a backdrop could Dr. Unger comment on the CDC website instructions which don't involve biological markers. Also, could she comment on research suggesting childhood factors are causative, and suggest psychiatric comorbidity. Could she comment on how some in the research community and patient population have expressed difficulty dialoguing with her.

Dr. Unger says the CDC website is "tried and true" information for the practicing clinician, it doesn't represent the latest research until it's better established. On the issue of significant but not essential bio markers, she agrees, and says this is exactly why she has been pushing for dimensionality and stratification.

Dr. Unger said early childhood stress has been published by the CDC and has been replicated as a risk factor for CFS and other illnesses. This early childhood trauma can take many different forms, and is one factor that is an indicator of modulating biology which can affect how a person responds to stresses of all kinds. The word stress isn't precise and is quite varied.

Dr. Jason follows up by asking her to clarify whether the CDC suggests that most with CFS have a personality disorder; some read the CDC publications to suggest this. Dr. Unger said she stands behind the CDC's research, and explains that the lack of communication results from the fact she is an acting chief in a period of significant transition, and it is difficult for them to make long-range plans and decisions, so she felt reaching out was not appropriate at this time.

Mr. Krafchick reminded the CDC of the insurance implications of the standardized definition they are looking for. Many claims are denied on the grounds the CFS is a mental health condition and he suggests that any criteria should be written to reject this view. Dr. Unger clarifies that the 1994 definition was not a CDC definition and they will not unilaterally make a definition, the CDC's role would be to coordinate a consensus definition.

Mr. Krafchick wondered what the time frame was for this, and Dr. Unger said this process was in a very early stage, and thinks the best way forward is to start with the data on differences in instruments and methodology. Dr. Unger replies to Mr. Krafchick that they will incorporate the Canadian criteria as part of the process. Dr. Klimas clarifies that this definition is the International Clinical Case definition, they only met in Canada. The research definition has a different function to this clinical definition.

Dr. Klimas asked for an update the education campaign to reach the primary care and provider community to make people aware of CFS and what the diagnostic criteria are for CFS, given that most with the disease are undiagnosed. Dr. Klimas describes this as a "health crisis". Dr. Miller said another Continuing Medical Education (CME) course is being planned, and said he could update at a later meeting. Dr. Unger said they are committed to education, and one recent improvement has been translating their website into Spanish. The toolkit they have published is being sent to local and county public health groups.

Dr. Hanna, Associate Director for Special Projects and Centers, Office of Research on Women's Health, National Institutes of Health

- Described her contribution today more as reflection than a formal report, and said she was sorry her term was finished because she is retiring.
- Remarked that the NIH has been responsive to the CFSAC suggestions, and would continue to be with new representation by Dr. Dennis Mangan, leadership, and organizational structure.
- Expressed that she was impressed with the science day, and thought it was a kind of preview to their three-day state of knowledge coming up in the spring, which would deal with the issues raised in greater depth.
- Pointed out that many who spoke were NIH researchers.
- Announced that Dr. Stuart Legrice who spoke on the science day on XMRV is joining the CFS working group at NIH.
- Responded to calls for networks or collaborative arrangements with researchers by stating they've been trying to set up such a network, have had meetings, but require money to follow through on this.
- Described the wealth of research available by the NIH, which addresses many of the questions that have been raised, and is even quoted by advocacy groups in

their arguments for better treatment of the disease. Will be staying on in a consulting capacity.

EXTRAMURAL CFS RESEARCH AT NIH

Dr. Mangan, Senior Research Advisor, Office of Research on Women's Health, NIH

- Explained that he will be having a panel discussion describing how NIH solicits more research applications which brings funding. All the panelists are members of different institutes or centers at the NIH, and are members of a trans-NIH CFS research working group (to be referred to as the working group).
- Stated that the NIH is composed of:
 - 27 different Institutes, Centers, and Offices (ICOs)
 - An intramural program where research is done at the desk or bench level at NIH.
 - A far larger extramural program, to which the panelists belong.
- Will request name change for the Trans-NIH Working Group to CFS/ME or ME/CFS, based on comments he has heard from patient advocacy groups at this meeting
- Stated working group purpose is to solicit, stimulate, support, collaborate, and coordinate research. It also communicates findings and fosters interaction and exchange of ideas on CFS.
- Make up of group includes the 16 key NIH institutes, 20 program officials, and there is growing interest amongst other groups.
- Presented brief history of working group accomplishments on CFS, including productive meetings, an RFA (request for application) and a PA (program announcement).
- Described 2011 plans, which include:
 - attempting to improve communication, which had been an issue, by improvements making for a more accessible informative website
 - NIAID (National Institute of Allergy and Infectious Disease) study on the association of XMRV with CFS patients, which will be detailed more by a subsequent panelist.
 - State of knowledge workshop on CFS.
 - Working Group Meetings to drive planning on the workshops, funding announcements and plan conferences.
- Once information from all of this was compiled it would be escalated to all relevant leadership to get commitments for funding.
- Said panel discussion would show how NIH supports diverse CFS research, as well as the NIH clinical XMRV study.

- Provided contact information in light of letter writing campaign going to a number of others at the NIH, which has distracted people from necessary work.
- New division director, Dr. James Anderson has shown personal interest in CFS and the working group.

Cheryl McDonald, Division of Cardiovascular Sciences, National Heart, Lung, and Blood Institute (NHLBI)

- Stated she would be restricting her presentation to the extramural component of the work that the NHLBI was involved with.
- Listed different mechanisms for funding grants, which are only for peer-reviewed research:
 - Research Project Grant - a discrete project grant for up to five years
 - Exploratory & developmental Research Project - a grant for up to two years for more preliminary research
 - Program Project Grant - these are large grants with multiple projects, reviewed internally in NHLBI
- Noted they are strongly supportive of fostering career development for early stage investigators, and provide training/career developments for pre and post doctoral candidates. Some pay for medical school, and one awardee is working on CFS.
- Cited prior grants on circulatory dysfunction, orthostatic intolerance and autonomic nervous system dysfunction in CFS.
- Stated that when NHLBI research is required, they will issue institute initiated proposals. This is an established, three step process:
 - To plan and develop initiatives based on input from the scientific community and other constituencies, and must meet the mission and plan of the NHLBI, and should complement existing investigator-initiated research. If they are deemed worthy they progress.
 - The board of external experts reviews the proposal, and prioritizes the initiatives at each round.
 - The NHLBI advisory council then reviews the prioritized proposals and makes recommendations to the director of NHLBI.
- In this particular economic funding environment, they have to weigh the fiscal resources and the program needs. Because of NIH's strong commitment to investigative research, the number of initiatives they can fund is limited.

Dr. Simone Glynn, NHLBI

- Focused on what the NHLBI has been doing related to research on XMRV in terms of blood safety, when research suggested there may be a threat.
- Stated they immediately created a Blood XMRV Scientific Research Working Group, which aims to design and support research to determine the threat of XMRV to blood safety. The group includes a wide range of relevant experts and federal agencies. She chairs this working group. They have participating laboratories at the CDC and FDA.
- Described the various investigations they pursue when a potential blood safety threat arises.
- Ensure they have reliable assay(s) to detect the agent.
- Determine if a proportion of the blood donor population have the agent.
- Determine if it is transmitted by transfusion.
- Evaluate if transfusions are associated with the development of the disease in the recipient population (5 million patients).
- Describes the current study, called the REDS-II XMRV Study, supported by the Retrovirus Epidemiology Donor Study, an institute-initiated program to improve the safety and availability of transfused blood projects.
 - There are four studies making up the REDS-II XMRV study:
 - Testing of analytical panels by the participating labs. This is complete.
 - Evaluate clinical sensitivity and specificity of assays. They are exploring what the best way of preparing the samples, what blood they should test, what timing is best. This is underway. They plan to release the results immediately so the optimal way of preparing samples can be known.
 - When more is known on sample preparation they will conduct a study on clinical sensitivity/specificity panel.
 - Determine the prevalence of XMRV in blood donors, which hopefully will be done early 2011.

Dr. Chris Mullins, Director of Urology Basic Cell Biology Programs, NIH Division of Kidney, Urologic and Hematologic Diseases, NIDDK

- Stated that NIDDK's mission on neurologic pelvic pain syndromes has begun to overlap with CFS, and they are working to understand the relationship between these disorders.
- Explained that Urologic Chronic Pelvic Pain Syndrome (UCPPS) has a hallmark symptom of chronic urogenital pain. These symptoms have significant morbidity and decreased quality of life, and even with much effort there are no effective treatments or identified risks.

- Explained that some progress had been made, including UCPPS comorbidity with fibromyalgia and CFS. This suggests that these could be systemic disorders.
- Described how NIDDK charted a new more multidisciplinary approach in response to limited success, called the MAPP (Multidisciplinary Approach to the Study of Chronic Pelvic Pain) research network, which looks into systemic problems potentially involving multiple disorders.
- States that they are using novel approaches, and a broad range of experts, including experts on CFS.
- The MAPP network has developed new protocols using cross network studies, as well as beginning new site specific pilot studies.
- These protocols are not stand-alone studies, but are integrated to provide a multilayer approach examining disease. Patients with one condition will be tested for other comorbid conditions, and will be phenotyped so they can be subgrouped. They are also looking to focus on flares in symptoms.
- Stated that the findings in future applications will encourage internal and external investigators to be involved in the network.
- Said that it will also stimulate new research applications.
- The NIDDK will always look to work with CFS research to progress their common missions.

Dr. Cathy Laughlin, Chief, Virology Branch, Division of Microbiology and Infectious Diseases, NIAID.

- Stated they have supported work on CFS on the immunologic side, and are receiving many applications on XMRV.
- Advertised the link to funding opportunities on the NIAID website, and said most research they fund is unsolicited, but they do have two important program announcements alongside many other groups which support pilot research.
- Described their two significant reagent repositories, one meant for biodefense, the other for AIDS research. There are 64 XMRV related genetic clones and vectors in the AIDS related repository.
- Described the state of the NIAID study on XMRV.
- Spoke to the discordant findings on the association between XMRV and CFS, and described the various reasons why this might be so. The NIAID study will incorporate NHLBI's REDS II studies' findings on sampling methodology etc (phases 1 and 2 previously discussed).
- Prospective identification of CFS patients from four geographic areas in US.

Dr. Mangan gave a brief summary of the different presentations. He focused on the MAPP network and said this is a promising model for CFS/ME.

COMMITTEE DISCUSSION

Dr. Glaser was pleased with the level of contact with the NIH at this meeting, and he expressed appreciation for their attendance. He said he was troubled by a couple elements. He asked if it was fair to say that the issue of XMRV was a long way from being settled, so why were other viruses being excluded? Why not include HeHV-6 (Human and Simian) and EBV (Epstein-Barr virus) since they have been linked to CFS? Also, If XMRV turns out to be related to CFS, is that the end of the story? What happened to the other viruses that have data to support them? Mentioned that the advocacy groups at the meeting had spoken about the reduction in research dollars on CFS, and the number of applications on CFS is decreasing, because the chance of funding is so low.

Dr. Glaser also spoke about his own experience working on CFS over the course of many years, including many studies. He never applied for NIH grants because he thought that those reviewing applications don't feel like there is a strong enough link between CFS and EBV, so it'd be a waste of time. After assembling all the data, after all those years, he did make a grant proposal to the NIH, it went to the special emphasis panel, got scored but didn't get funded. They discovered that amongst all the people on the special emphasis panel reviewing the grant, only 15 percent had any significant knowledge about EBV, and none regarding CFS etiology. The majority of people on the special emphasis panel were dentists or specialized in pain in the jaw. He found this disturbing.

Dr. Jason thanked the panelists for their involvement, and was excited to see program officials at a CFSAC meeting for the first time. He congratulated Dr. Mangan for being the first public official to use the term ME/CFS.

Dr. Jason asked Dr. Mullins about the MAPP network on pelvic pain. How did he get it going? Dr. Mullins explained that they wrote a funding opportunity announcement and publicized it well across multiple communities with the support of advocacy groups. They contacted dozens of investigators, lots of information meetings, and they established the review group before they funded the first application. Review wasn't difficult, the challenge was to get everyone to cooperate and communicate, especially between clinicians and researchers.

Dr. Jason asked how the NIDDK got to the point where they were resolved to invest in this area. Dr. Mullins responded that they have a traditional interest in pain, both in basic science efforts and clinical trials. They were already committed to studies, but had failed at attempts to build integrated sites so they tried a different approach.

Dr. Cook, following Dr. Glaser's comments, asked why almost all CFS applications go to the Special Emphasis Panel (SEP). Having been on the panel himself, he knows it's loaded with pain researchers and devoid of fatigue experts.

Dr. Hanna said they have recommended if people want their applications reviewed in other sections that they write a cover letter, and it was the CFS community that wanted the panel set up in the first place. Dr. Cook mentioned that it has significantly changed since that time.

Dr. Laughlin said that before submitting any application, they should contact the program officer, and you could mention if there was an issue with the SEP roster; they could send the application to a different section. Dr. Cook said that if you write a CFS grant, you aren't sure who your program officer would be. Dr. Mangan responded that the working group team would be working on making this process more clear, using the website. Dr. Cook asked if they could emulate the success of the MAPP network, and seek assistance from multiple institutes to be involved, and get a different, more diverse SEP. Dr. Mullins said a special review panel was established for this, and this was essential because of their new approach. Dr. Hanna said that more money was necessary to put out an RFA specifically for a MAPP-like approach for CFS.

Dr. Klimas said a difficulty with establishing a network was having a patient base large enough, which couldn't be achieved only at academic centers. It could be accomplished with the help of clinicians threading in patients, and they need those with knowledge of the topography of the disease to help with this. The network should also have a broader mission, and education needs to be incorporated into their thinking about the development of a network. Science will follow money, and there hasn't been much money, especially since they have difficulties as an interdisciplinary field.

Ms. Christine Williams said that any network interested in the intersection of research and practice could build on two existing networks at AHRQ. One is a primary care research network, the other is an action network.

Mr. Krafchick was surprised that CFS, irritable bowel syndrome (IBS) and fibromyalgia came up in doing research and networking in the context of the urologic group. Commented that there is no focus at the NIH for new systemic problems, and that it's ironic, or even backwards that CFS research came by way of urology, that the tail was wagging the dog. He echoed previous comments that the grant review process needs attention.

Dr. Glaser liked the idea of a CFS emphasis panel, but the people on it need to know what they are reviewing. Some weren't aware of this issue at the NIH.

Dr. Houghton asked Dr. Laughlin about the funding of XMRV pilot trials through the mechanisms she outlined, and followed up on Dr. Glaser's concerns about EBV being left out, saying there was promising research on antivirals on EBV and related viruses being useful for CFS. What is needed is a larger study to determine the effect. Could the NIH work with the private sector to develop drugs for CFS? Dr. Laughlin said yes, this was possible, but a clinical trial needed to come in as a pre-proposal, submitted to an institute committee, and these are quite costly and difficult to get approved. On public-private partnerships, it's also very difficult, but Dr. Laughlin said while it wasn't unusual, it's up to the applicant to seek out the private support in advance and apply together.

Dr. Marshall asked what the processes and criteria were for determining the rosters of the SEPs. What will Dr. Mangan's approach be to influence the construct of these SEPs to make them more appropriate. Dr. Mangan said it's based on the expected applicant pool, and this is further reason to contact your program director early.

AGENCY PROGRESS ON RECOMMENDATIONS (CONTINUED)

Deborah Willis-Fillinger, MD, Office of Health Equity, HRSA (Health Resources and Services Administration)

- HRSA's primary goal is to build a strategic plan which is quickly improving access to quality of health care services, strengthening the health care workforce, building healthy communities and improving health equity as cross-agency priorities.
- Noted areas of potential interest to those in the CFS community:
 - Bureau of Primary Healthcare is receiving significant support from the ACA. They are looking at 20 million lives currently covered through programs, doubling in the next three to four years.
 - A re-organization of that particular bureau might be of interest because their Federal Register Notice indicates priorities will be to identify key training and technical assistance needs of programs and staff. They aim to coordinate the Bureau of Primary Healthcare's training and technical assistance within HRSA across HHS and other federal agencies, states and local governments, and other public and private organizations concerned with primary care. Ultimately the goals are to eliminate health disparities and improve health status. This is a brand-new re-organization with staff specifically targeting and focusing on technical assistance and training needs of those new and growing community health centers and staff, and staff expertise will be part of that focus.
 - ACA authorizes a new national workforce commission. The focus will be developing recommendations to HHS to tool the workforce of the future to match the populations and the needs that are anticipated going forward.
- Included under the workforce commission:
 - Potential for research in model curricula to help support the workforce specifically focusing on individuals with disabilities and other populations, and to look at the curricula to be used by health professions schools and continuing education programs. Programs that would come out of this commission have not been funded yet but may be funded in the future.
 - Rule making committee which will define health profession shortage areas, medical shortage areas, and underserved populations, which will help decide allocation of resources. Committee is named and already meeting.

- CHARN was announced (Community Health Applied Research Network). ARRA funds made available to this for research on patient-centered studies.

Marc W. Cavaille-Coll, MD, PhD, Medical Officer Team Leader, Division of Special Pathogens and Immunologic Drug Products

- Highlighted events of July 26, and July 27, the 98th meeting of the Blood Products Advisory Committee.
- The Committee was updated with information on XMRV which is already on the CFSAC web site. The Committee will continue to follow this area very closely and look forward to finding more clarity based on the information that will be provided from studies outlined today by the NIH.
- Drug development activity for CFS remains fairly limited. Until there is a mechanism or etiology, or in vitro or in vivo models allowing researchers to select molecules might have an effect in this area, it is very difficult to start drug discovery and development. FDA remains interested in all the information heard today and will continue to follow the field.

Christine Williams, Director of Strategic Partnerships, AHRQ

- AHRQ develops and synthesizes evidence. There have been discussions with NIH regarding evidence synthesis for CFS. There may be a timing issue with regard to the spring meeting.
- Noted regardless of whether XMRV becomes the avenue they want to pursue, the fact that it was on the Washington Post has raised awareness among the public and gives legitimacy to CFS as a real illness and has served that purpose.
- Stated her commitment and would welcome conversation with anyone who wanted to speak to her.

Ms. Perry, CMS

- Represents CMS, works at the CMS Center for Strategic Planning, where she is the Assistant Senior Advisor for the Deputy Administrator responsible for overall strategic planning to the agency.
- Said she is personally focused on issues related to Medicare and Medicaid beneficiaries with disabilities and disabling chronic conditions as well as those eligible for Medicare and Medicaid. CMS (the Center for Medicare and Medicaid Services) administers the Medicare and Medicaid programs as well as the CHIP program for children. They have a significant role in implementation of the ACA.
- There are updates on web site WWW.CMS.GOV.
- A new administrator was appointed this summer, Dr. Don Berwick, who is currently in the process of working on new strategic planning process. Dr.

Berwick's key goal is to focus on improvement of patient care, improvement of population health, and reduction of cost.

- Encouraged ideas to improve service delivery and said there is receptivity for stakeholder input.
- Noted that the recommendation from May meeting regarding a demonstration project on patient care for CMS patients will be taken back to CMS. A demonstration project program is longstanding. A number of demos can be accessed on the web site.
- Many demonstrations were mandated specifically by the ACA.
- ACA set up Center for Medicare and Medicaid Innovation or CMI. CMI will be available January 2, 2011, in startup mode. She read from the statute what the goal is. "The purpose of the CMI is to test innovative payment and service delivery models to reduce program expenditures under Medicare and Medicaid while preserving or enhancing the quality of care furnished to individuals under such titles."
- CMI will be establishing mechanisms for stakeholder input into types of innovations to be tested, but isn't sure they will be disease-specific models.

COMMITTEE LUNCH

PUBLIC COMMENT

The following section highlights key points made by witnesses who testified during the public comment session. Access to the complete text of witnesses' written testimony is available at: <http://www.hhs.gov/advcomcfs/meetings/presentations/10122010.html>

Heidi Bauer

Shared testimony of a friend not able to be present:

- Friend is 56-year-old emergency physician diagnosed with CFS, atypical Lyme disease, and atypical MS (Multiple Sclerosis); her daughter is diagnosed with CFS, and chronic Lyme disease.
- Believes illness is of retroviral origin, both she and daughter test positive for XMRV.
- She has improved immensely from retroviral therapy, so has her daughter.
- Started a blog because patients have no help to share experience with treatment and clinical ideas. The response has been enormous of pain, neglect and abuse.

- Feels that since CFS patients do not die from this disease for a long time and so there is a tendency to feel there is no hurry. It is a progressive disease. Patients are too sick to wait.
- Stated they need compassionate care and are denied basic care and common decency for decades.
- Asked where have the epidemiologists been all this time? It is a travesty that clinical trials have not begun, and it brings shame on the medical profession.
- Remarked that the WPI has single-handedly made things happen for patients, why are they not funded?
- Wondered what CFSAC actually does. The committee is supposed to advise the Department of Health in reference to CFS matters. With the entrance of XMRV into the game, she hoped the Committee would be proactive in urging immediate funding. Instead, they left out two of the world's most renowned retrovirologists.

Lisa Baldwin (via telephone)

- Believed the medical board and insurance companies have such a powerful grip on this illness in North Carolina that health care becomes unattainable.
- Stated that when children have CFS, parents are blamed instead of those systems that discriminate against this illness. It creates roadblocks to effective and costly research and therapies.
- Once medical care became unattainable for her son, they audio taped the medical establishment's discriminatory resistance in providing medical care. Urged people to protect themselves.
- Munchausen's by Proxy is used as a tactic to withhold care.
- Medicaid in North Carolina is horrendous. She believes families suffer with this illness and are challenged by the medical system.
- She will fight everyday for every CFS patient until the research comes out in defense of CFS.
- Stated need massive reform, legal support, funding and effective programs to stop abuse of children.

Andrew Bokelman

- Described how he has struggled with CFS, and further contracted oral and prostate cancer.

- Stated concerns about talk of sample contamination in XMRV. Instead of digging in and offering on-point criticism, the sample contamination talk remains at a superficial level.
- Suggested that the contamination theorists start answering the hard questions and stop behaving as if holes in their theories don't exist.
- Argued that XMRV should be vigorously pursued. Suggested that the contamination theorists start answering the hard questions and stop behaving as if holes in their theories don't exist.
- Said that theorists should work cooperatively with people who are getting positive results and see why tests are coming out differently to further research and move along faster and find an answer sooner.

Rivka Solomon (video testimony)

- Rivka Solomon protested in front of HHS, demanding funding for clinical trials now. Suggested others do their own mini protest. Some of her testimony was presented in silence in the form of written placards.
- Stated that every year she is deeply disappointed by total failure of support.
- Stated that the name is belittling.
- Urged that new, promising XMRV research be supported with funding.
- Stated that the NIH spends \$31 billion annually in medical research for the American people but CFS research only received \$5 million. Please dedicate more money to researching CFS and the retrovirus XMRV. Dedicate more money to clinical trials so treatments can be found. Protect the Americans who have yet to get XMRV from blood transfusions, because this retrovirus is surely already contaminating the nation's blood supply.

Kim McCleary

- Introduced herself as president of the CFIDS Association of America (Chronic Fatigue and Immune Dysfunction Syndrome). CFSAC is very important to the community.
- Kim McCleary was proud that many of the presentations heard were started or sustained in some way by CFIDS.
- Observed that the common theme in moving testimonies she hears is that patients and scientists want CFS to be a mainstream medical concern met with the level of research funding, clinical attention and societal concern.
- Urged that Committee charter be changed to develop agenda that identifies the most important ways that each agency could perform its mission in the context

of CFS. Even though a change did not make it into the new charter, it is entirely consistent with its purpose.

- Strongly recommended development agenda that identifies the most important ways in which each agency could perform its mission in the context of CFS and a cohesive research agenda that would propel scientific momentum that has accelerated over the past year with the increased attention and focus for XMRV.
- Described the transformational opportunity for the Committee to make bold recommendations that form a progressive, inspirational agenda for immediate action with long-term impact for every person living with CFS and those who have given themselves to solving CFS.

Ken Friedman

- Introduced himself as treasurer of the International Association for CFS/ME, and listed the various organizations he was involved with.
- Expressed concern that Dr. Reeves questioned validity of XMRV findings for scientific reasons in the New York Times. Stated that while all federal employees have a right to express their personal opinions, they should refrain from doing so when they are being interviewed in their official capacities.
- Expressed alarm that studies showing links between CFS/ME and XMRV are being stopped from publication by senior public health officials.
- Argued that because programs are run by the Federal Government and paid for with taxpayer dollars it is the responsibility of those agencies to publish those results promptly.
- Argued that results of research sponsored by the Federal Government should be published independently of the research findings of other institutions and agencies.
- Requested that CFSAC fashion a recommendation to the U.S. Secretary of Health affirming that from this day forward the science conducted by any agency under purview and under the purview of any successors will be conducted to the highest professional and ethical standards of science.

Charlotte Von Solas

- Detailed her history with CFS without remission of symptoms for 20 years.
- Thanked Committee and thanked Dr. Mangan for changing name to ME/CFS, also thanked Dr. Anderson for his interest, and hoped leadership change would reform NIH thinking and action on CFS.

- Expressed frustration with Dr. Unger’s remarks on CDC definition of disease, which doesn’t describe anyone she knows with the disease.
- Stated that the Canadian Consensus Criteria is a good definition, and one of the things it stresses is exercise-induced relapse. Noted that there weren’t any changes made to accommodate this in the CDC definition since the last time this committee met.
- Suggested at the very least that ME/CFS and fibromyalgia should be separated. She feels the Committee can go a lot further and include immunologists and infectious disease doctors.
- Stated that CFSAC must demand an audience with the Secretary of HHS.

Joseph Polchinski

- Described deteriorating condition due to CFS
- Effects of CFS on him:
 - Physical Effects:
 - digestive, cardiovascular, muscular, urological and weakened immune system;
 - Financial
 - Drained his money and his earning potential.
 - Was laid off due to disease.
 - Health care is impossible to access.
 - Psychological/Quality of Life:
 - His life has stood still, no social life, no hobbies.
- Recommended a name change, more research, and to seize the opportunity to give life to people with CFS.

FAREWELL SPEECHES

Dr. Snell thanked those cycling off the committee and honored the short tradition of giving them the opportunity to say goodbye themselves.

Dr. Hartz

- Stated that CFSAC has a family feeling along with expertise and quality of teamwork and real commitment.
- Noted that people have expressed frustration with what the Committee has accomplished. One possibility for not accomplishing is the Committee does not have big enough ideas or push hard enough. Some ideas get presented and many do not because they do not think they will go forward.

- Described the fundamental problem as getting buy-in from the people we want to advise and not sure of the solution.
- Stated he would like to meet with the Assistant Secretary of Health and apparently that will happen and that will make a big difference.
- Asked for clarity in what was really wanted from the Committee. He feels it would be helpful to know what recommendations they want to have and what recommendations they don't want and have a consistent message about the Committee role.
- Stated that the Committee needs an understanding of what we are doing and why we are doing it in order to become effective.
- Described the mission as vague which makes the Committee less effective.
- Detailed that an area of improvement is on meeting structure. The speakers are virtually always interesting and informative, but it isn't easy to tie in what they say to the purpose and needs of the Committee.
- Expressed frustration when speakers arrive and there isn't an opportunity to discuss and refine what they are saying.
- Core environment is good with an incredible group with good ideas and strong commitment, but needs to be sharpened and better relationships outside the Committee fostered to get some buy-in and get some direction.
- Discussed that he and Dr. Glaser had discussed resignation due to lack of progress, but knew that the Committee was committed.
- Thanked the Committee for letting him be involved and expressed sympathy and hope for those suffering with CFS.

Dr. Glaser

- Described nadir of experience with the Committee when he found out their recommendations were not even being read, and thought about resignation.
- Described how he stopped research on CFS but restarted after attending a meeting, due to the testimony of those suffering from CFS, and said that those on the Committee are trying very hard.
- Commended Dr. Jones for taking control and turning the committee around with energy, excitement, and effort. Dr. Jones can make the meaningful changes for this Committee. Also commended a number of other Committee members for their efforts.
- Defended Dr. Miller who took heat regarding the CDC and really tried very hard to deal with the fallout over CDC, very supportive and did the best to deal with an uncomfortable situation.

- Ended by stating he will miss the Committee and feels optimistic.

Dr. Jones talked about the scheduling for the next meetings, which we will try to work around the NIH meetings, and nominations for vacated positions.

COMMITTEE DISCUSSION: FINALIZE RECOMMENDATIONS

Dr. Jones noted that Dr. Beth Unger had joined the meeting. Dr. Miller had to return to Atlanta.

Dr. Snell outlined the process, they'd read all recommendations, and if they are considered appropriate a motion would be made followed by a discussion and modifications if needed.

Dr. Klimas

First, some background was provided on motion 1. The Education and Quality of Life Subcommittee was focused on education and the disability materials reviewed in the meeting, as well as the advances in research and patients' wishes to see clinical trials begin.

The Subcommittee felt a clinical trial structure needed to be put in place. This process has been delayed because of the under-recognized and under-served patient population without access to health care. These issues could delay clinical trials networks at experienced research sites and could affect the size of groups to draw upon.

Motion 1

"Following other successful network models for complex diseases we propose the development of national research and clinical network using regional hubs serving as patient care, education and research hubs to fill a crucial need for the ME/CFS community. This network would make multi-disciplinary resources expanding access to expert patient care, assisting patients in disability assessments, developing educational initiatives and certification programs providing the core support for much needed research in clinical trials networks and providing experts to develop health care policy.

We believe that such a puzzle that integrates clinical medicine with basic translational and clinical trials research will address urgent needs with respect to ME/CFS including physician education to train skilled practitioners and expanding access to medical care for patients in different regions of the country and for the hundreds of thousands of patients that are in need of care. In translational and clinical trials research will rapidly move new knowledge to proven successful clinical treatments.

Research has been hampered by a lack of large databases that would allow sub-type analyses and focused-treatment approaches. This can only be accomplished by establishing national networks. The national network would standardize recruitment efforts as large databases are collected. Clinical education and care will hub regionally from these settings which will fill an (inaudible) need for patient care throughout the United States and monitor effectiveness of standard and research treatments for patients with ME/CFS. This innovation will reduce costs currently incurred by emergency care and specialty care treatment bases and treatment models and disability and loss of workforce contributions that often occur with those afflicted by delays of treatment of this debilitating illness.

Before we expect the chair of the CFSAC will engage in regular discussions with the Under-Secretary, the present Dr. Koh in order to develop ways to implement this recommendation. Both sub-committees will be fully informed of these negotiations in the spring meeting of the CFSAC will be the place where plans could be vetted by the entire committee."

Dr. Jones commented regarding terminology used in the motion. It was noted that the department abandoned the use of the term 'Under Secretary' and now uses 'Assistant Secretary for Health'.

Dr. Jason noted that the Research Committee strongly supported this motion and that it captured the essence of discussions held during this meeting and meetings of years past. Dr. Jason noted that Dr. Deborah Willis-Fillinger had advised that project officers from different institutes were in accordance with the same issues discussed and that it showed the importance of having this type of network assembled. He indicated that the time for action is now considering the groundswell of support and the strong interest level.

Mr. Krafchick noted that he has been involved with these issues with people with CFS for over 20 years and felt it was important regarding research to identify the patients in a consistent way so they can be studied and helped. The centers would make it easier to standardize and generate patients who could be studied for the purpose of research and obtain answers to unknown questions. That area he strongly supported. The education of medical students and practicing doctors was key.

Dr. Marshall countered that as a medical school faculty member he noted that the remarks of Mr. Krafchick were correct in principle but in practice probably upended. Change had to come from outside in. He felt that medical school faculties would approach it like scientists and skeptics asking whether ME/CFS is really an illness or only in the patient's head, similar to the issues expressed during the meeting. He felt that this problem would be resolved by patients going to their physicians explaining symptoms and asking the provider to help. The providers would then be the first to be

initially responsive. The difference would be that to the provider it would no longer be theoretical but practical, faced with the demands of their patients.

He thought there should be a strong emphasis moving backwards from the graduate medical education and then ultimately into the required curricula of the medical schools. He noted that usually it would only go into the curricula once the cause or science is understood, otherwise it could for instance, end up in psychological curricula.

Mr. Krafchick noted that with the centers he felt that it would attract educators who would teach others. He felt that medical schools should consider including information about ME/CFS in their curricula in some fashion. He agreed that the major force may come from people in the community treating the condition.

Dr. Klimas confirmed that the concept of education integrated into the model was a key portion of this proposal. She stressed the importance of hubs providing infrastructure support to the network of providers in the community. This would allow outreach into clinical practices and some core guidelines. This would facilitate the identification of some of these patients for clinical study.

Dr. Levine stated that the hubs could be used to circulate information to primary care physicians. Students could also be rotated as part of an externship and add to published research in the field.

Mr. Krafchick noted the importance of hubs, a place where physicians could refer patients.

Dr. Snell noted that the condition itself was extremely interesting in that it has many facets which may attract doctors to it for study.

Dr. Willis-Fillinger asked whether the models that were proposed could be used as centers where clinicians could refer patients. Dr. Klimas confirmed that this could be one of their roles. She noted that she does video consultations in her own practice at the VA hospital. Dr. Klimas expressed the view that it was an excellent education tool because she might see the patient first through video and in a following visit with the primary care physician. Management plans were then done in a cooperative manner. She noted that it was an excellent way to train primary care doctors. She also had used Skype in the video consultations. That whole area had strong educational elements.

Dr. Klimas described how some patients came in with excessive paperwork from other doctors and specialists and this represented a great deal of cost. However using their model it could be done more efficiently thereby improving it.

Dr. Jones confirmed that Medicare has had demo projects on telemedicine, telehealth, tele-mental health—so economies of scale and payment have already caught CMS's attention. She agreed that if clinicians worked together out of hubs it could only be more effective, to see someone in real time as opposed to waiting three months for a face-to-face appointment.

Dr. Levine asked whether the hubs would partner with an existing hospital or would stand alone. She gave an example of a hospital that she knew where the administrator

did not want to open a clinic to treat CFS. Dr. Klimas confirmed that there were many ways that individuals could become part of a center, from the academic world or areas of medicine and also that universities for example might pay physicians and a clinic within a university setting would help offset costs for the university. She felt most universities would welcome such a protocol as it would add to their portfolio. She suggested that it would be beneficial at some universities to group services more to make them more efficient rather than just having an array of services.

Dr. Jason thought that there was considerable agreement among the group, and it was in line with the ideas of advocacy groups as well. He thought that they needed to approve the motion and decide what steps were to be taken to make it happen.

Dr. Jason requested a vote and then an exploration of what next steps could be taken before they proceeded. Mr. Krafchick, among others, disagreed and noted that everyone should finish speaking before they moved ahead. Dr. Jason withdrew his motion.

Eileen Holderman confirmed that the motion was comprehensive. She had a clarification regarding the name of the center. She wondered since the MAPP initiative is very inclusive to overlapping syndromes and illnesses are the hubs to be envisioned as a place where conditions such as fibromyalgia patients or MCS (multiple chemical sensitivity), or Gulf War Syndrome patients would go?

Dr. Klimas said that the purpose of the meetings was really to try to develop and get the framework established and then hope that within that process that experts would be brought to the table and it would be discussed, but couldn't imagine leaving these out. Mr. Krafchick said that in line with the urology groups MAPP network, he saw no reasons why their proposal couldn't be inclusive of these other diseases/syndromes, many of which are comorbid. Others agreed with this more systemic model.

Dr. Snell suggested that at this point they were not in a position to make any distinctions and that many of the decisions would be up for further discussion. He asked if there were no major objections and took a vote.

CFSAC unanimously approved motion 1.

Dr. Jason asked that now the motion had been approved what steps would be put into action to have it implemented, he didn't want to just get stuck with the theoretical.

Dr. Klimas

- Responded to Dr. Jason's question by saying this was answered by Motion 2.

Introduced Motion 2. The concept behind this motion is the idea that this is an exciting time for healthcare due to the ACA, and they needed to be involved immediately. Experts should be brought in, as health care reforms are happening. Many changes are occurring, so how do they engage as experts now? There is a need to make sure it happens this year. They want to engage experts as participants in the process.

Motion 2

Dr. Klimas summarizes motion 2 as “We would like to ask HHS to engage experts from the CFSAC or other experts, as consultants or participants in the process as policies are changing.” They should engage the HHS early in the process.

Dr. Levine said that the MAPP network process involved a lot of leg work in finding receptive centers, and that they needed to do this same sort of work. Dr. Klimas said that the working group would do this, and if they involved CFSAC this would be useful.

Dr. Snell said that he would speak to the Assistant Secretary about this. Dr. Jones mentioned a number of sympathetic agencies that could be worked with. Mr. Krafchick saw a number of new opportunities that could be pursued, just mentioned within the meeting.

Dr. Hanna said that the CTSA (Clinical and Translational Scientific Research Center Awards) make a better model than MAPP, are already supported by the NIH, and had a history of supporting CFS. She pointed out that in MAPP the diseases get “lumped in together” with pain as the only organizing factor, and urged caution. Dr. Jones agreed that the CTSA had better resources, said that people were looking to MAPP as the model, but you could get there building on CTSA networks, as a different way to the same end.

Dr. Willis-Fillinger asked for clarification on how the funds flow for CTSA awards, do they come from one place. Dr. Hanna said the funds come from appropriations for the initiative, they weren’t from a variety of different centers pooling.

Dr. Jason called a vote.

CFSAC unanimously approved Motion 2.

Motion 3

Dr. Jason introduced another motion. He asked that the term ME/CFS be legitimized to encourage the use of the term and assist in the recognition of the illness.

Mr. Krafchick seconded the motion. He added the reservation that he had concerns about the damage it would do with people applying for benefits. But as long as CFS was in the title and this was adopted by the federal government it would overcome that concern.

Dr. Hanna noted that the NIH usually refers to the disease as ME/CFS, however the NIH had received requests to remove the ME from that name as it was creating complications for their organization.

Dr. Snell said there is significant bile associated with the distinction. He had some reservations about the name as it might change in the future, and though it might seem like a waste of time, it was so important to many patients. For that reason it would be worthwhile to go ahead with it at this point in time.

Eileen Holderman considered this issue one of respect for the patients. The name is also tied into funding. She thinks that when it does have a more scientific name it will generate more respect but also funding. But for the present time she agreed with the name change.

Dr. Marshall said adding ME to acknowledge it right now was fine as an interim name, but he was concerned that it might get lost as some sort of comorbid condition of another more recognized disease, and they had to be careful about that going forward. It had to be a defined illness with however many etiologies there end up being.

Ms. Holderman asked whether it was a matter of changing the name of the Committee. Dr. Jason clarified that it was more of an idea of endorsing and acknowledging and legitimizing the term, in terms of the field as it stands now; that it had become part of the discourse. Ms. Holderman agreed, and said it was an issue of respect and funding.

Dr. Marshall asked for confirmation that the motion was ME/CFS, not CFS/ME for the sake of consistency. That was confirmed. He also asked whether the term ME would be defined, due to the controversy over -itis vs -opathy. Dr. Jason said they would be avoiding it by leaving it as an acronym.

Dr. Jason called a vote.

CFSAC unanimously approved Motion 3.

Dr. Jason proposed Motion 4.

"We are concerned about the lack of progress in implementing the CDC's five-year plan. We want a more detailed progress report of what has occurred and what is planned. We recognize an important transition is occurring and there is a need for bold, new and creative leadership for the CDC's CFS program. After the new leadership is appointed we would like the new branch chief's plans to operationalize the entire five-year plan."

Dr. Klimas considered that is a statement as opposed to a motion. Dr. Klimas thought that it was something the Committee could request to the CDC when there is a new branch chief.

Dr. Snell thought that that would likely happen when the new chief came. Dr. Marshall added that the new branch chief should be invited to the next meeting to present or discuss the five-year plan.

Dr. Jones thought that it was a given that once the new branch chief was chosen that they be invited so that they were aware of where the Advisory Committee stood on issues. Dr. Unger said that as far as she was aware it was the CDC's intention to have ex officio representation on a higher level than branch level, but instead at a program level.

Dr. Jason removed his motion as it was not seconded. He asked that with remaining time they could ask further questions of the remaining ex officios.

Dr. Jones noted that the recommendations would be posted on the website and added to the tracking sheet. Transparency was important and that it be noted who was responsible and whether any action had been taken and also whether any progress had been made. She noted that the public and committee members should know that this information was on the CFSAC website.

EX OFFICIO FOLLOW-UP COMMENTS

Dr. Jason asked Dr. Cavaille-Coll why studies of the drug Ampligen, which has been known to treat CFS/ME, is not a priority for the FDA compared to the HIV/AIDS epidemic. What can we learn from how AIDS drugs got expedited approval.

- Noted example of Mary Schweitzer who suffers from this, has attended several of these conferences in the past in a wheelchair and this time actually walked to the podium to speak. She has been taking Ampligen.

Dr. Marc Cavaille-Coll

- Indicated that FDA merely provides guidelines to the pharmaceutical companies that do the actual testing of any drugs. Drug development is initiated by other parties.
- Cannot comment by law on the status of any investigative new drug, application etc. that hasn't been approved.
- Stated that there was a real identifying agent in the HIV virus, which made it easier to get drug approvals faster. We're dealing with a complex systemic disease in CFS which complicates things.
- It was mentioned that education is key. CFS does require medical attention.
- Said FDA experts doing the review understand the seriousness and severity of this illness. Experts in all types of these policies should be and are involved. The review process involves chemists, toxicologists, and other experts in this field. It

was mentioned that the reviewers should also be available for discussions, questions.

- A research clinical trial is needed and the studies submitted to FDA by the reviewers.
- There is only one path to approval; it doesn't matter if a drug is used in a different application.

COMMITTEE DISCUSSION

Dr. Houghton requested information on FDA process because it would help the committee better understand the steps involved from research to drug approval. His understanding was that drug X was approved for an indication in disease Y, not to "treat" in some general sense, disease Y. The FDA is specific about the margin of a therapeutic claim. Dr. Cavaille-Coll declined to confirm this because the process was more complicated, and referred Dr. Houghton to the website to see the more detailed approach.

Dr. Houghton said that his understanding of the rapidity of approval for HIV was commensurate with risk, even though this was denied, and there was no formal directive on this. Was more latitude given for conditions that had high morbidity?

Dr. Cavaille-Coll said they do take into account a risk-benefit analysis, and if there is uncertainty it can be taken to an advisory committee.

Dr. Klimas asked if they found a subgroup of CFS defined by a biomarker, under a certain threshold, that it would come under orphan guidelines. Dr. Cavaille-Coll said this would have to go to the office of orphan drugs, but there are not two different tracks entirely, they go through the same process but certain provisions are allowed if they are designated as an orphan drug.

Dr. Jason asked if Dr. Cavaille-Coll had any information beyond just the best practices and official stance that he could reveal in terms of how CFSAC could dialogue with the FDA.

Dr. Cavaille-Coll said they could speak to the review divisions their product would fall into and seek advice, or the Office of Special Health Issues, which has met with the CFS Committee in the past. Dr. Jason asked whether it would be worth CFSAC meeting with someone in the Office of Special Health Issues, and could he make introductions and alert them to the seriousness of the issue. Dr. Cavaille-Coll said that he isn't authorized to be a conduit to the agency as an ex-officio member, he is chiefly supposed to inform the Committee in its deliberations.

An unknown person in the audience began shouting to make their displeasure known with Dr. Cavaille-Coll's stance.

Dr. Jones clarified that other Ex Officios share the information they receive, and that it is helpful if he can "grease the skids" before she, as a Designated Federal Official,

approaches FDA with a request. She expresses disappointment with the idea that he would be unwilling to go back to the FDA.

Dr. Cavaille-Coll said that he does bring back information from the Committee to relevant interested parties at FDA. He apologized, said he was being misunderstood, and said that a number of products for CFS were across a number of different divisions, and that information about approval was publicly available, and perhaps he could find information that was more didactic to help. He said the FDA had a lot of outreach on education about their approval process, even if it had not done so with this Committee.

Dr. Snell asked if there was a formula or rubrics to determine what the risk was for a particular disease. Dr. Cavaille-Coll said that there was no set formula, it was all evaluated on a case by case basis.

Dr. Marshall indicated that when Dr. Jones spoke with the FDA, she would have to combat the ignorance about the severity of the illness. Dr. Jones said that she didn't have any sense that the FDA didn't take the drug seriously, Dr. Jones said that there is a regulatory process that isn't transparent and often there isn't sufficient proof, or issues with the way a study is designed, and there is a dialogue between FDA and the sponsor which others are not privy to.

Dr. Marshall said that the society undervalues the seriousness of CFS, and this may be impacting the risk reward analysis. Mr. Krafchick said it seemed the best avenue was perhaps to deal with Hemispherx, who produces the drug.

Dr. Klimas expressed doubt that experts were reviewing drug safety and efficacy. Dr. Cavaille-Coll said that they do get experts in the field, and that they do understand the severity of the disease, but have seen little development in the area due to lack of understanding on the etiology and pathophysiology that allows companies to identify promising products. They are welcome to anyone who has a promising product.

Eileen Holderman asked whether there were written guidelines on CFS that they consult. Dr. Cavaille-Coll said there is no specific manual for CFS or indeed many other products.

Dr. Jones asked again whether there are specific definitions or thresholds for safety and efficacy that guide any analysis. There is no formula for that. The products need to show efficacy and are based on well controlled trials. The controls could include active controls.

Dr. Jason asked who the reviewers are at these critical stages. For approved products, there are none. When a product is approved, the information on the reviewers is provided. Dr. Klimas said she felt like Marc was "getting hammered" by the questions and in defense described the helpfulness of the FDA in an experience she had had, and described the process as "extraordinary." Only one drug has only ever tried to go through for CFS, and we are holding that up as reason to criticize the FDA. There is much work to be done on their end before they can criticize the FDA. She believes when they are ready they will find the FDA to be expeditious. Dr. Jones furthered this by

describing the FDA as some of the “finest scientists in the world” and suggested that the group move on.

Dr. Jason asked whether the names of reviewers are made public record. Dr. Cavaille-Coll said that when a product is taken to an advisory committee, it is usually the reviewers who present their findings to the committee. The briefing package submitted is sent to the members of the advisory committee and is made publicly available. The advisory committee's website will usually identify the speakers and the authors of these reviews. There will always be discussion with the companies at every step along the way to share with them and provide advice as to how to assure their product has the effect they intended.

Dr. Snell said it might be appropriate to bring a science officer from Hemispherx in and discuss things with them to learn more, before allocating blame.

Dr. Houghton asked whether guidelines could be provided for drugs without an etiologic agent. Dr. Cavaille-Coll said that the FDA would provide guidance as an application progressed depending on what aspects of the disease it dealt with. He is hopeful that the science will change to enable more products. Dr. Cook pointed out that some drugs have been approved based on patient outcomes alone. Dr. Cavaille-Coll acknowledged that these were a factor in approvals as well.

Dr. Jason said that these long periods of discussion were really helpful, and should be allowed for in future meetings.

It was suggested that, in preparation for future meetings, if there are specific topics members would like the FDA to discuss, to inform the Committee in advance.

ADJOURNMENT

The Chronic Fatigue Syndrome Advisory Committee was adjourned by Dr. Snell.