The Twentieth Meeting of

THE CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE

US DEPARTMENT OF HEALTH AND HUMAN SERVICES

Hubert H. Humphrey Building, Room 712E, 200 Independence Avenue, SW
Washington, DC 20101

Tuesday, May 10, 2011 – 9:00 am to 5:00 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
Jordan D. Dimitrakov, MD, PhD	Boston, MA	05/10/10 to 05/10/14
Eileen Holderman	Galveston, TX	05/10/10 to 05/10/14
Michael Houghton, PhD	Danville, CA	05/10/10 to 05/10/14
Leonard Jason, PhD	Chicago, IL	04/01/07 to 04/01/11
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

Agency for Health Research and Quality

Christine Williams
Director of Strategic Partnerships

Centers for Disease Control and Prevention

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

Center for Medicare and Medicaid Services

Alaine Perry, M.P.H.
Senior Advisor for Disability and Special Need
Population
CMS Center for Strategic Planning

Food and Drug Administration

Marc W. Cavaille-Coll, M.D., Ph.D.
Medical Officer Team Leader
Division of Special Pathogens and
Immunologic Drug Products

Heath Resources and Services Administration

Deborah Willis-Fillinger, M.D.
Senior Medical Advisor
Office of the Administrator, Center for Quality

National Institutes of Health

Primary
Dennis F. Mangan, Ph.D.
Senior Research Advisor
Chair, Trans-NIH ME/CFS Research Working Group
Office on Research on Women's Health
Office of the Director

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

Social Security Administration

Primary
Cheryl A. Williams
Director
Office of Medical Listings Improvement

Alternate
John Federline
Deputy Director
Office of Medical Listings Improvement

EXECUTIVE SECRETARY

Wanda K. Jones, Dr.P.H

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Agenda

9:00 a.m.	Call to Order Opening Remarks Roll Call, Housekeeping	pg	Dr. Christopher Snell *Chair, CFSAC* Dr. Wanda Jones *Designated Federal Official*
9:15 a.m.	Agency Updates and Progress on Recommendations: CDC, HRSA, AHRQ, FDA, CMS	pg	Ex-Officio Members
10:00 a.m.	State of the Knowledge Workshop-Outcomes and Committee Discussion	pg	Dennis Mangan, NIH Committee Members
11:00 a.m.	Break	pg	
11:15 a.m.	Public Comment	pg	Public
12:15 p.m.	Subcommittee Lunch	pg	Subcommittee Members
1:15 p.m.	Discussion of International Classification of Diseases-Clinical Modification (ICD-CM) concerns	pg	Committee Members
2:15 p.m.	Committee Discussion	pg	Committee Members
3:15 p.m.	Break	pg	
3:30 p.m.	Public Comment	pg	Public
4:30 p.m.	Committee Discussion and Plans for Day 2	pg	Committee Members
5:00 p.m.	Adjourn	pg	

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Call to Order

Dr. Christopher Snell, Chair, was presiding.

CALL TO ORDER/OPENING REMARKS

Dr. Snell welcomed committee members to the CFSAC (Chronic Fatigue Syndrome Advisory Committee) spring meeting. He commented on the recent NIH (National Institutes of Health) State of the Knowledge Workshop and said it generated a lot of energy. He expressed a wish that momentum could be maintained through the next two days and used as a springboard to make meaningful improvements in the lives of people with CFS (Chronic Fatigue Syndrome).

Dr. Wanda Jones conducted the Roll Call:

Opening Remarks

Roll Call, Housekeeping

ROLL CALL

Committee/Voting Members Present:
Dr. Christopher Snell, Chair
Dr. Dane B. Cook
Dr. Jordan D. Dimitrakov
Eileen Holderman
Dr. Michael Houghton
Dr. Leonard Jason
Mr. Steven P. Krafchick
Dr. Nancy Klimas
Dr. Susan M. Levine
Dr. Gailen Marshall Jr.

Committee/Voting Members Absent:

Liaisons/ex officios Present:
Dr. Marc W. Cavaille-Coll
Dr. Dennis F. Mangan
Dr. J. Michael Miller
Alaine Perry
Christine Williams
Dr. Deborah Willis-Fillinger

Liaisons/ex officios Absent:
Dr. Janine Austin Clayton
John Federline
Cheryl A. Williams

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Staff/Others Present:
Dr. Donald Blair
Dr. Basil Eldadah
Mr. Timothy Gondre-Lewis
Dr. Wanda K. Jones

Staff/Others Absent:

Dr. Jones

- Informed visitors about building facilities.
- Commented on the increased visibility of the committee with website improvements. Stated that the bylaws were posted. Noted that these bylaws provided the procedures that support CFSAC activities.
- Stated that members would be hearing about the outcomes and findings of the State of the Knowledge Workshop held in early April at the NIH. Noted that as part of the workshop Secretary Sebelius sent a greeting to the participants and the Secretary's letter was posted on the CFSAC and the Trans-NIH ME/CFS (Myalgic Encephalomyelitis) Research Working Group websites and copies were available.
- Noted *ex officios* from three agencies would be rotating off due to retirements or changes in responsibilities and new agency representatives had been identified and would be introduced at a later time.
- Noted that they had nominations for new committee members. Explained that they were scheduled to lose six members within a 15 month time period. Stated that because of this they requested that the CFSAC leadership including Dr. Snell, Dr. Nancy Klimas and Dr. Leonard Jason be extended for one year. Stated they had two nominees that they had put forward. Advised the extensions were approved by Dr. Howard K. Koh who had that authority and in addition were officially approved for one year. Explained this allowed them to maintain continuity and develop a plan for handoff for the committee and sub-committees.
- Advised that of the two new members one was present at the meeting and this was Dr. Jordan Dimitrakov who would join them at the table after he was officially sworn in. Advised that the second member was Dr. Anne Vincent who was currently out of the country but would be sworn in soon which would enable her to participate in sub-committee meetings.
- Noted that they were pleased that Dr. Ronald Glazer and Dr. Arthur Hartz would be replaced by two very talented members.
- Explained the processes concerning public testimony.
    - It has to be made compliant with the disability adaptive equipment. Explained that this takes time as it is completed in batches and forwarded to be posted to the website.

  - All testimony received at the meeting and persons speaking today should ensure a written copy of their testimony is sent in and all of it is posted as part of the public record.
  - Testimony is limited to five pages. Testimony received in excess of this would be cut off at five pages or the person providing testimony would be asked to shorten it.
  - Responded to requests for testimony to be removed from the website after posting by explaining that because this is a public meeting published in accord with government sunshine requirements, everything that the public or presenters might present must be made available. Requests could be made that a person's identity be labeled anonymous or testimony made under an assumed name. Those requests must be made ahead of time. Once posted it is difficult to go back because of caching on the internet.
  - A new process is in place to try to expedite public comment. There were 50 requests for public comment, so there is a long wait list, and they want to try to get to as many people on this wait list as possible.
- Noted the website is heavily used and over three months they are approaching 10,000 page views and these were record levels. They are constantly looking to improve the website and welcome suggestions.
- Advised that they had hired the Deputy Assistant Secretary for Women's Health, the Dr. Nancy Lee who was there in the audience. Noted that that the responsibility for the CFSAC resided in the Office for Women's Health. Noted that Dr. Lee was getting more familiar with the issues so they would be looking at some additional optimization of procedures as they went forward. Explained that they were always looking for ways to improve the public's access to what they do and improve the public trust and how they use public money.

Agency Updates and Progress on Recommendations: CDC, HRSA, AHRQ, FDA, CMS

AGENCY UPDATES AND PROGRESS ON RECOMMENDATIONS: CDC, HRSA, AHRQ, FDA AND CMS

CDC – CENTERS FOR DISEASE CONTROL AND PREVENTION

Dr. J. Michael Miller, Centers for Disease Control and Prevention, National Center for Zoonotic, Vector-born, and Enteric Diseases, *Associate Director for Science*

- Congratulated Dr. Dennis Mangan and the NIH on the State of Knowledge Workshop. The CDC participated in the workshop and a scientific presentation was made entitled, "The Genomic Studies of Chronic Fatigue Syndrome."
- Gave an update regarding publications:

  - Since the last meeting the CDC has had two publications accepted, one on the economic impact of chronic fatigue syndrome in Georgia on direct and indirect costs and the other on convergent genomic studies to be published in the Journal of Neuropsychobiology.
  - Six abstracts were submitted for the IACFS (International Association for Chronic Fatigue Syndrome) meeting that will take place in Ontario in September and several have been accepted as oral presentations.
- Gave an update on education and outreach:
  - They are engaged in addressing patient concerns about their web content on the CDC site. They added an expanded section on disability in CFS completed in March emphasizing social security issues.
  - The Spanish translation of the CFS webpage was launched in October of 2011.
  - In February and April they participated in teleconferences with CFIDS (Chronic Fatigue and Immune Dysfunction Syndrome) association and one of the things that Dr. Unger and her group are beginning at the CDC is the planning of small group meetings with patient advocacy groups. The first one is with PANDORA (Patient Alliance for Neuroendocrineimmune Disorders Organization for Research and Advocacy) scheduled for later on in May.
  - Also developing two new CME (Continuing Medical Education) courses for 2012. The proposed courses will incorporate CDC's e- learning initiatives. The first course is entitled, "CFS Clinical Diagnosis and Management" and the second is "CFS and Sleep."
  - CDC has a program called COCA (Clinician Outreach and Communication Activity) and they are investigating the possibility of using COCA for provider education. Tentative plans include developing a simplified message and guidance to primary care physicians and work with nursing schools beginning with the Atlanta area, later to expand.
  - They have initiated discussion on the potential metagenomic collaborations for pathogen discovery in CFS samples.
  - Ongoing data cleaning and analysis for three large studies, one the follow-up study of "CFS and Chronic Unwellness in Georgia." The other is the "The Pathophysiologic Mechanisms of CFS" and then "The Registry of Unexplained Fatigue, Illnesses in Chronic Fatigue Syndrome: The Pilot Study."
  - Finalized an agreement to make CFS studies available through the Research Data Center at the CDC. This data would be available to the public and they have added appropriate controls to assure the required compliance with human subject protection.
  - The annotation of The Wichita, Kansas clinical data is on target for launch by the end of FY11. The goal is to make the data sets public and available to all researchers.
  - They have initiated the acquisition phase for some contracts to gather standardized data on chronic fatigue subjects from three to five different clinical practices with the purpose of

informing future discussions they will have regarding the case definition. The contracts will be about $100,000 each and if funding continues the working group could form the basis of some collaborative studies they hope to initiate.

- Noted that the outcomes of the contracts with the clinical practices would be to provide a forum for dialogue among clinical investigators about issues relating to diagnosis and management of chronic fatigue, including best practices for clinical management and to develop a consensus on key instruments and variables to stratify chronic fatigue patients and to ascertain the extent of patient heterogeneity between practices.

- Introduced Dr. Ermias Belay who was in the audience and who would be taking his place after the meeting. Noted that Dr. Belay is a physician, an epidemiologist at the CDC. Added that he was the Associate Director for Epidemiology Science in the National Center for High Consequence Pathogens and Pathology in which the chronic fatigue program resides. Stated that Dr. Belay brought a lot of experience and would be an asset to the committee.

HRSA – HEALTH RESOURCES AND SERVICES ADMINISTRATION

Dr. Deborah Willis-Fillinger – Office of the Administrator, Center for Quality, *Senior Medical Advisor*

- Congratulated NIH for a very interesting conference and was encouraged to hear of the science that is starting to come together.

- Stated that she asks the different bureaus and offices at HRSA for updates on issues they think might be of interest to the committee. Provided a summary of responses:

  - The Office of Special Health Affairs at HRSA has another office under it called the Office of Strategic Priorities and they have been studying the issues of depression and integration of appropriate screening in the primary care setting. HRSA and the Substance Abuse and Mental Health Services Administration (SAMHSA) have co-funded a cooperative agreement with the National Council for Community and Behavioral Health that will train providers around the bi-directional integration of primary care in behavioral health. This will help to train primary care providers in screening, detection and appropriate management of behavioral health and depression and train behavioral health specialists in primary care management.

  - Noted that 872,000 patients within the HRSA community-supported healthcare system were seen with a primary diagnosis of depression in 2009.

  - Discussed the health centers that promote preventative care and advance the medical health home model of coordinated comprehensive and patient-centered care. Noted that they recognize chronic fatigue as a complex disorder that requires early detection and entry into care and a coordinated care response through primary care teams. Noted that primary care and specialty including behavioral health specialists and rehab specialists are

important. Stated in order for health centers to be ready to care for patients with chronic fatigue the medical-home approach is the most efficient and effective.

- Provided an update on the HIV-AIDS bureau. Noted that 14 of the federally-qualified health centers at HRSA participated in the first cohort of a study by Robert Wood Johnson Foundation to pilot a program called "Project ECHO" which uses technology to extend the reach of specialists by training primary care providers and others to identify and manage or co-manage specific chronic diseases. Noted that these include high-burden diseases such as HIV, cardiovascular disease and behavioral mental health problems.
- Noted that the Office of Rural Health Policy (ORHP) has a program that might be of interest to the committee as rural communities are also affected. Noted that there are funds for rural health outreach, grants for training, screening, health fairs, education training for providers etc. in rural communities. Advised that it required a certain amount of data about the basic incidence of the disorders in the communities in order for funding to take place.
- The Maternal and Child Health Bureau (MCHB) had programs that might be of interest. Noted that they provide systems development funding to provide infrastructure for families with children with chronic illnesses including family to family counseling, access to medical homes, early and continuous screening and an information network to help families understand how to access resources.
- She discussed the Bureau of Health Professions (BHPR) and noted that in October it had been mentioned that there was a negotiated rule-making committee that was looking at the health professional shortage in medically-underserved populations. Noted that that committee was still working on this but will be completing their work in October of 2011. The group had members that represent the disabled community and are looking at issues concerning definitions for disabled populations. Noted that the formulas they decide will be important for allocating resources to communities in need of healthcare providers and resources.
- She mentioned that another program of interest is the Bureau of Clinician Recruitment & Service (BCRS) which had the responsibility for the National Health Service Core Program (NHSC). This involved 8,000 primary care providers and clinicians in daily contact with the NHSC through social network marketing to connect with providers. These networks could be used to share information on CFS with providers.

AHRQ – AGENCY FOR HEALTH RESEARCH AND QUALITY

Christine Williams, *Director of Strategic Partnerships*

- Thanked Dr. Mangan and the NIH and congratulated them on the State of the Knowledge conference held several weeks ago. Stated a number o f thoughts she had as a follow-up to the meeting:

- She noted that AHRQ did a synthesis on CFS in 2001 and that she and Dr. Mangan had preliminary discussions about the possibility of updating the synthesis. They were waiting for the final report from the State of the Knowledge Workshop. Stated that AHRQ is interested in working with other colleagues across the department on a possible update of the synthesis of CFS research.
- She noted that one of the things that came out of the workshop was clinicians and researchers connecting with each other, many for the first time.
- She stated that CFS is a complex illness with many symptoms and many systems of the body that are involved and so it is important to try to help facilitate dialogue between researchers in various fields working on CFS research as well as clinicians in practice. She elaborated giving one idea of AHRQ and other agencies supporting a learning network comprised of clinicians and researchers to continue the dialogue and improve connecting the dots between research and practice.
- She noted that as a secondary piece of such a learning network she has had discussions with Dr. Willis-Fillinger, Dr. Eileen Holderman and others about the possibility of the core network reaching out to others in primary care practice, primary care clinicians through a project like Project ECHO or something similar. She emphasized that although the talks were preliminary it was a concrete step to ensure people are talking to each other and that people are aware of research in other fields.
- The AHRQ was looking at programs that might benefit CFS patients and providers including some programs and tools for the management of patients with chronic disease.
- Ms. Williams mentioned that she is a CFS patient and was retiring from government because of the illness. She said that she does intend to stay engaged with the committee and with the work of CFS. She named her successor who is Beth Colin-Sharpe who is a PhD RN from AHRQ and she gave the opinion that she would be a great addition as the *ex officio* from AHRQ. She added that she was the point person for women's health at AHRQ and has experience with comparative effectiveness research and other fields.

FDA – FOOD AND DRUG ADMINISTRATION

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

- Advised that on January 24, 2011 the FDA made a decision on the assignment of drugs used to treat CFS. Noted that the Office for New Drugs (OND) used to have several panels assess new drugs but now they developed end points such as instruments that relied upon patient-reported outcomes (PRO). Noted that the development of such tools may facilitate development of new products to treat patients with CFS and allow better assessment of the benefits of products.

- Noted that the search for underlying etiologies for CFS continued and further research to understand the pathophysiology of the condition would also help in the development of new products.
- Noted that to work effectively with internal and external stakeholders on developing clinical trial endpoints, i.e. the PRO instruments designed for assessing symptoms and responses in CFS and critical trial designs, the OND leadership had agreed to assign all CFS applications to a single review decision, the OND, the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) Stated that this will allow for a coordinated and consistent process for review and the development of expertise in a specific area.
- Noted that effective January all new applications for drug and therapeutic biologic products for CFS would be assigned to DPARP.
- Compared the situation with 1992 when the OND did not exist, and the Center for Drug Evaluation and Research (CDER) had two offices in drug evaluation and six divisions. Noted currently they had the OND with six offices of drug evaluations and eighteen divisions. Noted that the products for CFS had diffused across many areas but now have been consolidated.
- Advised that if any parties wanted more information about DPARP they could refer to the FDA website at www.fda.gov then enter chronic fatigue syndrome in the search engine the first item that would come up in the search results would be the posting.
- Congratulated Dr. Mangan, together with the steering committee, for organizing the State of the Knowledge Workshop on CFS at the NIH attended by several members of the FDA.
- Noted that at the last advisory committee meeting there was interest expressed by some to learn more about the FDA. Noted that he would like to assist the members of the committee and the public to access information. Proceeded to give search techniques to locate areas on the site. Noted they have a website for consumer information for patients and patient advocates and the search words to put for that would just be "patient advocates." Elaborated further on what information they offer. Noted also the website on FDA basics accessible at www.fda.gove by entering "FDA basics" into the search box. Elaborated in detail on what areas and information that page would provide.
- Gave information about the Office of Special Health Issues (OSHI) at FDA which may be of interest to people with CFS. Noted that the OSHI served as the liaison between the FDA, patients, patient advocates and health professional organizations. Noted that the staff encouraged and supported participation of these groups in forming FDA regulatory policy. Explained that the OSHI responded to enquiries and concerns about HIV AIDS, cancer and other special health issues.
- Encouraged the members and the public to go to the FDA website and use the search engine to find different sites and explore the ways the FDA informs the public about CFS.

CMS – CENTER FOR MEDICARE AND MEDICAID SERVICES

Alaine Perry, CMS Center for Strategic Planning, *Senior Advisor for Disability and Special Need Population*

- Noted that CMS only just joined the committee in the fall and that they were very happy to be there.
- Gave some updates regarding CMS:
    - The CMS administers the Medicare and Medicaid programs and the Children's Health Insurance Program (CHIP) at the federal level.
    - They have a new responsibility of interest to the committee and advised that after the Healthcare Reform legislation passed last year the HHS created an entity to administer the private insurance pieces of the law to get up the health insurance exchanges and other coverage expansions related to private insurance and also to oversee the consumer protections and insurance reforms.
    - In January this entity was merged with CMS so they now have the responsibility for all those functions.
    - That office will also be dealing with the federal portion of assisting the states get the exchanges up and running to expand insurance.
    - There is an interim program of high-risk pulls that they have a role in implementing.
    - They also are involved in providing better information for consumers about health insurance options and they have a website with that information.
    - Also responsible for monitoring and developing the insurance reforms.
    - To access this information on their website the acronym is the CCIIO (The Center for Consumer Information and Insurance Oversight).
- Discussed their Innovation Center, set up under the Healthcare legislation which mandated the establishment of the Innovation Center within CMS.
    - Its role is to be aggressive about developing and testing and disseminating reforms to the healthcare service delivery and payment systems to improve care, care coordination and care quality and lower costs.
    - It investigates inefficiencies in the system currently where care is not coordinated and to leverage technology better.
    - It has two elements, changes in service delivery and also payment reform.
    - CMS is the largest health insurance payer in the country with Medicare, Medicaid and CHIP programs. Changes that CMS make in payment structures can influence how healthcare is

delivered including payment of things that are not currently compensated or well compensated like care management, care coordination functions, uses of technology.

- Some initiatives launched so far include demonstrations in medical homes, working with states to conduct demonstrations to better integrate care for dual-eligibles, and partnering with providers on patient safety reforms.
- Some differences with the Innovation Center are it does have dedicated funding through the Healthcare Reform Bill and it has the authority to implement changes if they can be shown to lower cost and improve quality.
- They are dedicated to looking at and improving areas where the service delivery system is currently failing CFS patients.
- The Innovation Center has a website which can be accessed at http://innovations.cms.gov There is a web portal for submitting proposals.

- Noted that the CDC has the lead on the ICD 10-CM development and implementation which would be discussed later in the meeting, but stated CMS has a significant role in implementing that, especially with educating providers on changes.

COMMITTEE DISCUSSION

Dr. Leonard Jason expressed concern that the presentations were excellent but there was very little time for questions and discussion. He noted that many of the speakers read their reports so wondered if it was possible for the reports to be sent, posted and then the time could be used for discussion.

Dr. Snell noted that it was his understanding that they had made changes and that they would forward questions to the *ex officios* and the *ex officios* were going to respond directly to the questions within the presentations. He noted that there was a breakdown and that had not happened. He agreed that it would be preferable to engage in discussions about specifics and they needed to ensure that that happened for next time.

Dr. Jones noted that if anyone was supposed to receive questions it was her and she did not receive questions from Dr. Jason. She apologized if this was the case and if her large volume of e-mail may have been the cause. She noted that there was time during the day for discussion and many of the *ex officios* would be available for discussion.

Ms. Eileen Holderman noted that she was in some agreement with Dr. Jason. She noted that Dr. Jones had mentioned that the *ex officios* did not want to be blindsided and had asked for questions ahead of time for that reason. She explained though that the panelists also did not want to be in that position when hearing the reports. She added that she had a number of questions after the presentations and also expressed the wish for the materials to be forwarded so they had sufficient time to read them before the CFSAC meeting.

Dr. Nancy Klimas stated that the presentations were very focused on what could be done and the next step was how they move forward? She noted that the information was new and relevant. She asked Dr. Cavaille-Coll about when the FDA is trying to develop outcome measures and who is informing the process? How can they be involved in that as the investigators, the scientists that do the work? If the FDA is going to try to develop a sense of it that they need to conform to, how do they do that?

Dr. Cavaille-Coll advised that there were several groups at the FDA interested in the development of PRO measures and he directed those types of requests for information to the DPARP. He noted there was a guide in 2006 posted on PRO's. He suggested going to the FDA website www.fda.gov and put in the search "patient reported outcomes" items will come up that would inform you about many presentations on the topic.

Ms. Holderman asked whether there was a special go-to person, or someone assigned to the CFS area.

Dr. Cavaille-Coll responded that she should contact that division and they would be able to answer that question. He noted that DPARP was in the process of receiving different applications from different divisions.

Dr. Jones suggested to the committee that if they are interested in patient reported outcomes they can work with the FDA to have a formal presentation dealing with what they are allowed to discuss , not what is behind the decision-making but more what is public about the process and what they're looking for including what the definitions are. She added that whatever the committee is interested in hearing from the FDA that they could work on identifying a presentation from FDA on that topic. She suggested it might be a possibility for the fall meeting.

Dr. Susan Levine asked Ms. Perry about the model she had suggested for coordinated care for CFS. She asked if she had suggestions on how to implement that. She noted the importance of electronic medical records which were an important incentive but was there some way that CMS was working with CFS to coordinate care with primary care providers, urologists, and cardiologists or is there a model?

Ms. Perry confirmed they were working on care coordination models more broadly. She noted that it wasn't specific to CFS but there were a number of different models being tested. She mentioned two of them, Medical Homes and Accountable Care Organizations, which are being both tested and implemented. Dr. Levine asked what is Medical Homes?

Ms. Perry responded Medical Homes was a basic model based in the primary care setting and it was responsible for care coordination. They could receive additional funding for care management fees and they tried to play a role in ensuring that they're tracking all the care with a specific patient, so there was an emphasis on providers working as a team.

Dr. Levine asked about the proposals she had mentioned regarding Medical Homes. Ms. Perry responded that there were a couple of the Medical Homes demonstrations that were currently taking place. She noted the website at The Innovation Center and they were soliciting proposals from the general public and noted the website was http://innovations.cms.gov

Mr. Steven Krafchick enquired further about the group Dr. Willis-Fillinger had mentioned that was looking at defining disability. Was this correct?

Dr. Willis-Fillinger responded that there was a negotiated rule-making committee looking at defining medically underserved areas, medically underserved populations and health professional shortage areas. These are all federal designations that help identify priority communities in need of federal support. The designation formulas which assist in resource allocation are being revisited right now, which is why she brought it to their attention. Mr. Krafchick asked whether this involved physical obstacles to getting to care, and Dr. Willis-Fillinger responded that it was in a very broad sense but she couldn't provide more detail as the work hasn't been finished.

Dr. Jason agreed that the presentations were rich in terms of opportunities for the committee to get a sense of what could be done for the field. He noted in particular the presentation by Ms. Perry and noted that there were a great number of people outside of the healthcare system with CFS and many patients were desperate. He asked if Ms. Perry could go back to her agency and obtain information about the economic cost to Medicare and Medicaid of treating people with CFS. He noted that it would help them to make a case to illustrate the economic burdens on individuals.

Dr. Jason asked Dr. Miller about the five-year plan and if there was a possibility of going back and looking at some of the objectives announced over the last year and a half and to see how close there were to reaching some of the objectives of the five-year plan.

Dr. Miller responded that looking at the objectives of the five-year plan would not be a problem. He noted it was currently being reassessed at the CDC. He noted as it was presented to the committee initially that the reassessment and the evaluation could also be presented to the committee.

Ms. Holderman addressed Ms. Perry. She noted she drafted a document about specific issues that CFS patients were having with Medicare and Medicaid and it highlighted five different issues and included a series of questions that Dr. Jason had alluded to about statistical data. She noted that it would be extremely helpful to get CMS to comment on this. Ms. Perry noted that she did not have a copy of this but would take a look again and see what they had. She recalled there were some questions they may not have data on but she would look into it.

Ms. Holderman asked Dr. Willis-Fillinger about the Bureau of Primary Healthcare section of the report in which she wrote that CFS is a complex disorder and then said it included primary care and specialties including behavioral health specialists and rehabilitation specialists. She noted that when she hears CFS there were many more types of specialists that came to mind for her; neurologists, endocrinologists, immunologists etc. Did she take into consideration those types of specialists? Dr. Willis-Fillinger responded yes, all specialties, but their programs primarily support primary care evaluation and referral, so there is less support for specialty services.

Dr. Snell noted that he was concerned about something three people had mentioned: the idea that once case definitions have been decided, when treatment information becomes available then they could move forward with education and clinical treatment. He asked is that really the case? And if so, what could they do to change the situation? Is the definition holding up the delivery of clinical services and training models? He noted he did not require a response at this time.

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State of the Knowledge Workshop- Outcomes and Committee Discussion

STATE OF THE KNOWLEDGE WORKSHOP – OUTCOMES AND COMMITTEE DISCUSSION

Dr. Dennis Mangan, Office on Research on Women's Health, office of the Director, *Senior Research Advisor, Chair, Trans – NIH ME/CFS Research Working Group*

- Thanked them for the opportunity to provide an overview of the Workshop held on April 7 and 8 on the NIH campus.
- He introduced several of the moderators from the conference, Mr. Timothy Gondre-Lewis from the NIAID, the National Institute of Allergy and Infectious Diseases, Dr. Basil Eldadah from the National Institute on Aging (NIA) and Dr. Donald Blair from the National Cancer Institute (NCI).
- Stated that he would provide a history of The State of the Knowledge and why it occurred when it did:
    - The Last State of Knowledge meeting was in 2003. Subsequent to that there was support for a conference to follow that and it was planned for 2010/11.
    - Noted it came together after he joined the committee as an *ex officio* member and he thanked committee members for their help and participation.
    - Formed a steering committee to develop the format of the workshop, the content and the speakers. He described the makeup of the steering committee.
    - The steering committee worked as a core to bring in information from the scientific community, patient advocacy groups, from the NIH institutes and from other *ex officio* members.
    - Established the three goals of the workshop: it would provide a snapshot, look at gaps in portfolios and look for opportunities.
    - Noted that it was not meant to be a research-agenda generating workshop or target any specific aspect of CFS. He noted that that would follow after careful analysis of the workshop discussions and subsequent consultations.
    - Regarding content, the workshop was composed of 32 science and clinical experts and had a strong emphasis on audio-visual communication, and reaching out to people who did not have a chance to go. It included investigators, patients and their families.
    - Noted that their IT staff advised that there were 900 people watching the workshop live with 100 attending the actual workshop. Attendees included advocates for the illness, scientific investigators and the media.
    - The webcast has been archived and is available.

  - It was divided up into ten sessions covering a range of topics on CFS/ME.
  - They created the sessions with overlap and there were no breakout sessions, everybody at the table participated.

- Provided a summary of some of the highlights:
  - It is clear that there is still a tremendous amount that they need to know about the illness and there is no consensus with regard to the cause, the diagnosis and the treatment for the disease.
  - One area that received a lot of discussion was the case definition. He noted there were many definitions and they lead to variable diagnoses for research subjects. He noted that research needed standardization.
  - The close relationship that exists between ME/CFS onsets to flu-like illnesses and suggested an infectious disease etiology or "trigger." Microbes were discussed including EBVs, enteroviruses and retroviruses and all remain candidates for triggers.
  - The discussion of XMRV was informative and controversial. There is debate about the association of the retrovirus and any retrovirus with the disease. They are hopeful that information coming from two large NIH-supported studies is helpful. These are the Lipkin study and the Blood XMRV Scientific Research Working Group.
  - Immunopathology and the complex interactions within the immune system and how they interact with other organs were discussed.
  - This discussion of the networked complex interaction of systems lead into their session on systems biology, a new area of research dealing with how you put clinical and basic science information into numbers, making it computer friendly and in digital format to make it easier to analyze trends.
  - They discussed neurology and talked about pain and the dysfunction of the autonomic nervous system and ways of providing new avenues of treatment for ME/CFS.
  - He highlighted a presentation on the neuroimaging of the brain, which showed that the brain activity in the CFS patient was clearly different from healthy controls. This could lead to an explanation of symptoms, especially cognitive and sleep disorders.
  - They discussed post-exertional malaise and it generated a lot of interest.
  - They discussed diagnosis and that led to the conversations about biomarkers.
  - Discussed biomarkers and how if correct biomarkers are obtained it could be very helpful but could also create problems if not correct.
  - They discussed treatment opportunities; there are many, and also many well-meaning physicians trying to do their best with limited information. Current treatments are aimed at symptom management. No cures have yet been identified.

  - There is the opportunity for networking with investigators and interdisciplinary research and using common resources.

- Noted that a final report was being generated from the workshop. Stated the working group is now going to pull the proceedings and notes from the scientific writers at the meeting and analyze them. That would serve as a launching point for ancillary activities that would occur.
- Noted that the working group would use the reports as a basis for discussions about and increase awareness for ME/CFS research across the entire NIH and the bio-medical community.

COMMITTEE DISCUSSION

Dr. Jason thanked Dr. Mangan for this work and stated that the process that was used should be a model for work that is done at CFSAC. He noted that it was important to note the process and not just the outcomes for the workshop. He asked about funding and whether an RFA (Request for Funding) might have been considered? He asked about the editor of an academic journal who requested an article which spoke to standards and how you would need to characterize a sample before you publish a paper. He wondered if establishing such a standard could be a challenge for the advisory group.

Dr. Mangan agreed this was the type of conversation needed to pull together the research community, to make them think as a collective unit. He discussed further the benefits of types of networking given that it was a relatively small field.

Dr. Mangan took to time to respond to the issue of funding. He noted that they were not in a position with the budget now or in 2012 to say they would be able to do this or that initiative. He noted that with experienced program heads they have learned how to build a program with limited resources by connecting researchers with opportunities for grant applications. The working group also helped to develop new professionals in the field. He noted if they received funding then they would be able to support new research, but until then they would press forward in those areas they could.

Dr. Dane Cook asked what is the best way for them as researchers and physicians and the CFSAC to maintain the momentum generated at the State of the Knowledge Workshop? How do we stay engaged with the NIH to ensure we don't lose any opportunities?

Dr. Mangan stated the folks at the meeting were part of a larger group of members and program officials at the NIH at various centers. He stated they want to have an open door and increase the accessibility of the working group to everyone. He thought that the working group was the best way to stay connected to the NIH. Dr. Mangan said how that contact was made, and what messages should be sent was a useful discussion.

Dr. Gailen Marshall brought up the reverse translational approach to research. Even, for example in the R21 exploratory awards (NIH Exploratory/Developmental Research Grant), feasibility data tend to be essential. The reverse translational approach was antithetical to this. He asked if there were other examples and other illnesses where this reverse translational approach -- where one proceeds from

diverse patient presentations -- has been used successfully for funding. Could it be constructed somehow in an educational format?

Dr. Mangan noted that one example could be autism where you would be working backwards many times, also in many chronic pain diseases like TMDJ (temporomandibular joint disorder) He also noted some other chronic pain diseases. Dr. Basil Eldadah also gave an example of sarcopenia, which was similar to CFS in that there was no precise definition. Dr. Eldadah described this effort and how there is an ongoing initiative which engages the NIH through a public-private partnership to establish a better diagnosis through biomarkers. This initiative brings together a number of stakeholders to tackle the issue. The initiative has been successful so far and has produced publications and other research efforts.

Dr. Klimas noted that there was an opportunity coming up at the IACFS (International Association for Chronic Fatigue Syndrome) meeting in the fall. There was enough time to formalize a networking workshop that might bring experts from the working group to the major group of investigators. Dr. Mangan noted that he would look into that and was headed to that meeting. Dr. Klimas expressed that their clinical data set could be linked as their genomic data set is linked, and this accessible data would be a far better tool. This could be done formally through the IACFS.

Dr. Klimas expressed frustration regarding inadequate guidelines for CFS. She described a situation where an insurance company could use research papers and cite them as a reason to not pay patient costs. Dr. Klimas gave an example where insurance would only pay for rehab or psychology, with all other CFS costs denied. She wanted to ensure that up-to-date research was disseminated to insurance companies, who were prejudicially using very old information.

Ms. Williams noted that her physician attended the workshop and he supported the concept of reverse translational research. She noted that he felt that clinical practice should inform the research agenda. She referred back to the original question of Dr. Cook and said, how could the momentum be maintained post-workshop? She suggested a facilitated-learning network, which the AHRQ has experience with.

With regard to Dr. Klimas' point, Dr. Jason mentioned that there are influential websites outlining best practices of 2011 which are stigmatizing. He thought the committee should inspect the websites and see if they have accurate information. Are they biased and are they stigmatizing the patients? He thanked Dr. Mangan for bringing officials from other departments. He noted that some officials from other departments are skeptical about CFS and this had been a problem for investigators. He asked each of the program officials about how they feel about this illness, and how is it considered within their institute?

Mr. Timothy Gondre-Lewis of NIAID spoke and said it was important to talk to your program officer and see what programs are out there. He noted that he had worked with Dr. Klimas and with a colleague of hers in formulating applications, and for these to have the best chance of funding, early contact with the program office was necessary. He personally felt this was something they wanted to see move forward.

Dr. Eldadah stated that at the NIA they were interested in chronic fatigue as older people experience fatigue so there may be some overlap in the mechanisms. He noted that conferences were a great way to develop networking and consensus building especially for areas that different programs would have

in common. Also mentioned the SBIR (Small Business Innovation Research)/STTR (Small Business Technology Transfer) grants as an underutilized opportunity.

Dr. Donald Blair from the NCI noted that the interest in fatigue was probably fatigue associated with the advance of cancer and the fatigue associated with the responses to therapy , and these are areas that the NCI has an interest in. He also noted the interest in some of the etiological agents listed and discussed at the workshop what agents are linked to CFS but have also been linked to various aspects of cancer.

Ms. Holderman thanked him for an excellent workshop. She said the interest generated is great but that there was a concern that this interest would lead people to websites that might be flawed and could cause negative consequences like insurance companies not funding care. She stated they would be taking a step backward if the websites did not reflect the advances in science. She suggested the websites be redesigned with updated content and this would be a huge step forward and not a costly one. Dr. Klimas echoed this, and said a website that reflected the current state of the science could be very helpful.

Dr. Michael Houghton thanked Dr. Mangan for the workshop. He noted that it was disappointing to hear him say he was unsure about future funding. He noted that they know funding is required to make advances at the clinical and research level. He asked how are decisions at high levels on funding for ME/CFS made? He said it would make sense to have a rational way to determine funding for illnesses afflicting Americans based on the number of people affected, the personal cost, and the economic cost to the country. This process did not seem to be occurring.

Dr. Mangan responded that based on his experiences with NIH sometimes funding decisions can start with shared conversations, e-mails and then usually a major meeting such as the State of the Knowledge Workshop which is used as a foundation. Then the institute becomes interested in aspects of that workshop. They would look at their institute's mission and then put together a summary, talk to supervisors, division directors and branch chiefs asking how they can move it forward. They then go to the next level of administrators. These higher administrators then suggest partnerships to push an initiative forward that would have funding. He noted that there was also politics involved.

Dr. Levine referred to the Lipkin study which got funded in accelerated manner. Did it matter that the topic was a retrovirus, something that sounds more compelling? And can she, a researcher, but not based at an institution, but with a private practice, have a good chance of getting an NIH small grant application funded?

Dr. Mangan said that yes, a hot topic can sometimes come to the media and result in a project getting funded faster. He noted that the normal turn around for an application is nine months. For the second question he said they would recommend that she get connected with a research community and then come in with an application. Dr. Levine stated that this was a big roadblock for an individual practitioner, as there weren't institutions in her area interested in the subject. Dr. Eldadah noted that if she had an idea she ought to call up the program officer and they would find creative ways to see how to get it funded.

Mr. Krafchick emphasized how important the website information is because about half of the health insurance companies have teams that focus on CFS, and if there is a website that is negative in terms of treatment or disability they would use that. They don't look for positive research.

Dr. Cook wanted to know the plan for the broad dissemination of the workshop information. How could they make credible information available? Dr. Mangan responded that it is archived right now. The executive summary being prepared now and will be disseminated to the public and uploaded on the websites.

Dr. Snell asked if it was a neutral summary or did the NIH make some judgment about the significance of the findings? Dr. Mangan responded it would be neutral . They do not take a position.

BREAK

The Chronic Fatigue Syndrome Advisory Committee recessed for a five-minute break.

Public Comments - Morning Session

PUBLIC COMMENT

Dr. Jones outlined the new process regarding the public comment queue, and time keeping for comments, with a view to accommodating as many comments as possible.

Jennifer Spotila (via telephone)

- Noted she had been ill with CFS for more than 16 years and had never been more hopeful.
- Noted that the NIH State of the Knowledge Workshop showcased the current state of research and identified key opportunities and challenges in the field.
- Thought the researchers appeared engaged, interested and ready to solve CFS. Dr. Francis Collins and Secretary Kathleen Sebelius appear to be paying more attention to CFS than previous officials.
- Stressed that a plan is necessary. Stated that researchers must communicate and collaborate across discipline silos. Thought the CFS case definition was a barrier to success and we need standardized data elements and outcome measures. Thought existing resources for data sharing and clinical networks must be leveraged.
- Thought the current federal budget climate requires creative leadership on CFS so progress can accelerate.
- Commented that CFSAC could play a key role in developing such a plan with the expertise and access to *ex officio* representatives from every relevant federal agency.

- Thought that high quality, rigorous and well-designed research was the only way to find answers. Thought that instead of traditional models, they needed new verbs in the CFS lexicon: coordinate, prioritize, innovate, share, strategize and act.
- Commented that there was political will to solve CFS and scientists were ready to collaborate on research. Thought a comprehensive plan was needed and hoped the CFSAC would undertake this crucial task.

Dr. Jones thanked Ms. Spotila and asked members of the public giving testimony that if they had not submitted their testimony in writing to do so. They could also hand a copy to any committee member.

Kimberly McCleary

- Stated she was the President and CEO of the CFS Association of America.
- Noted that it has been 30 years since people in small towns around Reno, Nevada and rural Western New York State came to the attention of their physicians. Stated that at first the patients were typical of others with routine acute-flu-like illnesses. Noted that they failed to recover after weeks and months it was clear that their illness was not routine.
- Stated that over those 30 years there had been a lot of water under the bridge for CFS. Noted that there was anger, disappointment, discouragement and despair in the CFS community right now. Noted that for those who had waited for answers to simple questions about CFS for years, the sustained lack of clarity about the role of XMRV (Exenotropic Murine Leukemia Virus-Related Virus) and other murine leukemia virus-related viruses was the latest example of research that has thus far failed to deliver.
- Believed that rigorous research is the only route to answers and improved methods by which CFS could be detected, diagnosed, treated, cured and prevented. Believed engaging more researchers from a broader array of disciplines and backgrounds was essential to understanding the disease.
- Stated that the Statement of Knowledge Workshop demonstrated how much had been learned about CFS but also demonstrated how little that knowledge had translated to better care for CFS patients.
- Noted that the CFIDS Association of America(Chronic Fatigue and Immune Dysfunction Syndrome) stands for rigorous research that would lead to better care for CFS patients. Noted the results of NIH-supported research in XMRV would provide answers about whether XMRV and was a route to better care. Stated they would support the outcome of those studies whichever way they lead.
- Stressed that CFS requires help and resources from federal agencies, organizations, and individuals. There must be a proportionate response to meet the large challenge.

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Keith Baker (via telephone)

- Thanked the committee for giving him an opportunity to speak and all the committee members for their hard work. Thanked Dr. Mangan for getting the workshop done.
- Stated that his family all remained ill after 24 years now and still there was no test, no treatment. Noted his personal experience with the disease, and described how his family all had symptoms suddenly, which suggested that it could be contagious. Noted that today he was able to work part-time and still suffered greatly. Said his sister could work off and on and sadly his brother could not work at all.
- Stated that what made it so hard to live with were the cognitive and mental symptoms; diminished memory and focus. He really noticed this on returning to school. He was a good student but afterward found paying attention in math almost impossible.
- Noted the lack of belief and the lack of understanding from doctors. Half of the infectious diseases doctors did not even believe in CFS. Noted that there was also a lack of support from friends and family, and lack of education and public awareness, and stated that all of these factors snow-balled.
- Asked what could be done? Noted CFS needed to be defined properly and asked for the use of the Canadian Consensus Criteria (CCC). Expressed the opinion that the CDC continued to study incorrect patient cohorts. Noted that cohorts of outbreaks need to be looked at also.
- Thought that the CDC definition should be abolished.
- Thought funding needed to be increased and put on par with illnesses such as MS that caused a similar amount of disability and suffering. Noted that excellent institutions were applying for grants and more consideration should be given. Thought panels should not be comprised of professionals such as dentists and psychologists.
- Thought that the high number of families with multiple CFS patients meant this should also be studied.

Dr. Fred Friedberg(via telephone)

- Thanked the committee for the opportunity to present public testimony.
- Addressed the recommendation process at the CFSAC. Noted the committee had put forward recommendations over the past years intended to advance recognition, funding and public policy initiatives for ME/CFS. Noted few had produced results with exception of the 2009 initiative to change the CFS leadership at the CDC.
- Noted they were cooperating with Dr. Beth Unger at the CDC on CFS research.
- Saw problems with complex, multi-faceted and far-reaching recommendations which were more difficult to reduce to practical particulars, for example the repeated calls for the Centers for Excellence, as they are expensive and politically difficult.

- Thought multiple recommendations that covered a wide array of issues were also less likely to show results because they lacked focus and are easier to ignore.
- Thought that with the State of the Knowledge Workshop there was an opening for constructive action. Thought that Secretary Sebelius recognized the CFSAC Chair, Dr. Snell for the recommendations of the October 2010 meeting. Noted that as a result CFSAC recommendations had been recognized at the highest levels.
- Thought that for the next step, recommendations should be clear, focused and concise, also realistic.
- Thought that a realistic recommendation was for a new NIH-based program announcement dedicated to funding CFS projects.

Pat Fero

- Indicated she was reading testimony for a 22 year old man who was bed-ridden, named Benjamin DePasquale. It is his fourth year with the illness.
- Stated that we needed the doctors and clinicians to be educated. Asked that people look at his experience to see how clinical ignorance could lead to disaster.
- Described how at 18 years old he had a bout of mono. Continued his education and was accepted into a program for industrial design. He woke up in April of 2007 feeling ill and later collapsed. Noted that the mono faded but symptoms stayed. Said the doctor was intent on believing that he was depressed. Saw a series of doctors in specialized fields and all tests were normal.
- Noted that in 2008 Dr. Bell diagnosed him with CFS. Stated that in 2009 his condition deteriorated and his father took him to the hospital. The doctor there transferred him to the psych ward. Described how he pleaded for some sleep meds but they encouraged walking.
- He spent four days in the psych ward and the symptoms increased tenfold. Was completely bedridden and dependent on his caretaker, his father and a nurse's aide.
- Noted that he could not sleep and felt like he was in a perpetual crash. Had body aches and his muscles burned constantly.
- Noted that there was a need to educate current physicians and recruit new doctors.

Marly Silverman

- Thanked the committee for allowing her to appear for PANDORA. Stated she was the founder of PANDORA, a small grass-roots charitable foundation dedicated to restoring quality of life for individuals with ME/CFS.

- Said their budget averaged $50,000 in the past three years but they were of national and international scope.
- Stated CFS patients are no longer invisible. Noted there was a sense of urgency and anger and defiance no matter what language was spoken.
- Stated that PANDORA urged them to continue to pursue and recommend a comprehensive and prioritized approach by the Department of Health and Human Services through the NIH, CDC, AHRQ, HRSA and other agencies for coordinated funding that would advance the current body of knowledge for ME/CFS.
- Acknowledged the excellent workshops, meetings and the fact that science was catching up regard to the disease but stressed that without the funding in place nothing could go forward. Stated the government lacked commitment to move the knowledge forward. This had been the case for decades.
- Noted that her button read "I'm am worth more than $3.64" and this button reflected the annual amount currently spent by the NIH on each ME/CFS patient.
- Urged the committee to use their influence to ask the NIH to provide funding to pursue and implement initiatives would push forward research.
- Urged the CDC to urgently review their website and take down incorrect research materials.

Meghan Shannon

- Showed a 1992 poster about ME/CFIDS awareness that had been shown around the world.
- Stated she had been coming since the inception of the inter agency meeting with Dr. Phillip Lee, and corrected that Dr. Phillip Lee was the Assistant Secretary to Health and Human Services who started the interagency meeting, and that they had had attention from higher ups in the past.
- Noted she co-founded the international organization for medical professionals, and had been involved since 1985.
- Gave details of hospitalization from the 1980s and medical details concerning herself and her sister. She recounted how she was infected with Adenovirus, a DNA virus.
- Stated that when XMRV research was discussed along with HTLV-2 (Human T-cell Lymphotropic Virus) like viruses, it made sense to her due to her background with the disease.
- Asked the CDC to correct their website. Gave an example of how publishers of a women's health book had sent a letter to the Obama team asking specifically about CFS, and it ended up being responded to by a pat answer from the CDC using information from 1993, even though they had specifically urged the transition team to adopt the recommendations of CFSAC.

- Expressed anger and frustration and said it was her last time coming to one of the meetings. Expressed appreciation to Dr. Wanda Jones. Gave details of her downward spiraling economic situation as a result of the illness. Advised she was 62 and had been sick since she was 33.
- Apologized and thanked the committee.

Cheryl Marshall (via telephone)

- Greeted the committee and thanked them for allowing her testimony. Stated she was too sick to attend. Stated she used to be an active person earning an income but it had all been stripped away. Stated her career had been taken from me due to ME.
- Expressed disappointment at the way numerous doctors had treated her and stated that many of them did real harm.
- Stated that she has 15 co-morbidities that she manages.
- Diagnosed with breast cancer but could not receive chemotherapy due to the weakened state of her body. Noted the cancer could now reoccur.
- Noted that sick patients should not have to be the advocates for the disease. Stated that more researchers and doctors should be working on our behalf.
- Noted that President Obama had made an announcement in a letter to ME/CFS patients and said he made $8.2 billion available to the NIH for medical research grants. Considering this, she asked why the ME/CFS budget was only $6 million.
- Asked that the appropriate money be allocated to ME/CFS.

Joseph D. Landson

- Greeted the members of the committee. Stated name was Joe Landson. Thanked them for allowing him to speak. Said he has been ill for six years.
- Stated his purpose there today was to give his endorsement to the use of cognitive behavioral therapy, also known as CBT.
- Stated that it was his belief that if clinicians, medical researchers and health administrators underwent a supervised program of CBT, they could have their incorrect illness beliefs cured.
- Provided some illustrations using props of how clinicians were not trained or receptive to learning about ME/CFS and recounted his own personal experience.
- Stated that we need to bring clinicians on board rather than view them as enemies. They need to give them information to make them allies and get them asking questions.

Mike Dessin

- Stated that last month's State of the Knowledge meeting seemed promising and hoped it was used as a stepping stone in research treatment and awareness for ME/CFS.
- Stated in his opinion the current state was not good, the lack of mainstream research, physician knowledge and public awareness remained the same as nearly two decades ago.
- Stated that he believed the name of chronic fatigue syndrome was the single biggest reason for lack of progress and the utter neglect and abuse patients experienced.
- Noted that there had been a lot of discussion about the name but there needed to be more discussion as the name chronic fatigue syndrome had made a mockery of a very serious and life-threatening disease, myalgic encephalomyelitis.
- Gave his opinion that although the trend was to call it ME/CFS they should not be mentioned in the same sentence.
- Encouraged the committee to recommend research into the phases of progression within one illness, myalgic encephalomyelitis.
- Stated that the definitions of CFS did not describe it, but there were distinct phases of ME. Gave an explanation using a chart and discussed subsets.
- Stated in conclusion that the committee should recommend abolishing the name CFS completely as it has caused a dilemma for ME patients.

LUNCH

The Chronic Fatigue Syndrome Advisory Committee recessed for lunch for one hour.

Discussion of International Classification of Diseases-Clinical Modification (ICD-CM) concerns

DISCUSSION OF INTERNATIONAL CLASSIFICATION OF DISEASES – CLINICAL MODIFICATION (ICD-CM) CONCERNS

Dr. Christopher Snell

- Brought the meeting to order. Noted they would have a discussion of the ICD-related questions and the proposed reclassification of chronic fatigue syndrome.
- Advised there was a page in the members' notebooks tabbed after the State of the Knowledge summary which noted key steps in the development of the ICD 10 CM, so a clinical modification of the World Health Organization's (WHO) ICD 10. It would replace ICD 9.

- Stated his understanding of the issues:
  - Disconnect between the way the U.S. uses the classification and the rest of the world.
  - The way CFS is classified under the ICD system has implications for both reporting of incidents, morbidity and mortality.
  - Used by outside agencies to categorize the illness for purposes of inclusion or exclusion.
- Opened the floor for discussion.

Dr. Wanda Jones

- Clarified that the committee requested that the National Center for Health Statistics have someone to talk to them about the international classification of diseases, about the process, about how the U.S. adapts the WHO index, the ICD for use and about opportunities for dialogue.
- Noted that a meeting was set a year ago for May 10 and 11 in Baltimore that engaged resources for the CMS, parts of the federal government focused on health IT and the entire ICD team from the National Center for Health Statistics (NCHS). Noted that as a result no one was available for the CFSAC meeting.
- In lieu of their attendance, she developed some questions that the NCHS, ICD team responded to.
- Tried to clarify the questions so they would have a good understanding of the key processes and the key inflection points differentiating the WHO process from the U.S. ICD-CM, the clinical modification process.
- Raised additional questions regarding how alignment from prior versions is maintained and how ICD coding is used in decision-making. Noted also the relationship between the coding and the diagnostic and statistical manual (DSM).
- Stated that the information was provided by the NCHS and is meant to generate discussion.
- Stated that the ICD-CM process is a public process with regularly scheduled public meetings. Noted that there is an opportunity to comment as part of that process and to engage. Confirmed that the NCHS stated that there has been no public presence from the CFS community at the meetings. Noted that this was the process for people interested in CFS coding to become involved.
- Confirmed that there was a lock procedure that is soon to be executed for the ICD 10 CM. Noted it had been in development for a decade and the United States' move to electronic records means it has to temporarily lock the codes. The electronic health records software would not be ready if they keep changing them.
- Noted that information about coding changes would continue to be collected, taken under advisement and the NCHS would continue the process of evaluating. Stated that once it is in

public use then that lock will release and there would be an opportunity on a periodic basis for updating.

Dr. Leonard Jason

- Stated that the committees are developing ICD 10 CM and it intends to retain CFS in R codes (R53.82) and this means that the symptoms, signs, abnormal results of clinical or other investigative procedures are ill-defined conditions.
- Stated that R-codes means it's an ill-defined condition regarding which no diagnosis is classifiable elsewhere. Explained that if it cannot be diagnosed elsewhere in ICD 10 it goes into a R-code.
- The intention in ICD 11 is to put CFS with two other conditions (post viral fatigue syndrome and benign myalgic encephalomyalitus) under a G-code, being G93.3 or diseases of the nervous system.
- Noted that coding CFS under the R-code in the proposed ICD 10 CM would place it out of line with the International ICD 10 used in over 100 countries. Discussed the problems and implications of the U.S. coding of CFS as compared with how other countries are coding it. It would exclude it from the R53 malaise and fatigue codes, which would imply that CFS does not have a viral etiology.
- Brought forward a motion to be considered:

CFSAC rejects current proposals to code CFS in Chapter 18 of ICD 10 CM under R53.82 chronic fatigue syndrome unspecified, chronic fatigue syndrome NOS (not otherwise specified). CFSAC continues to recommend that CFS should be classified in the ICD 10 CM in Chapter 6 under diseases of the nervous system at G93.3 in line with international ICD 10 in ICD 10 CA which is the Canadian clinical modification and in accordance with the committee's recommendation which we made in August of 2005. CFSAC considers CFS to be a multi-system disease and rejects any proposals to classify CFS as a psychiatric condition in U.S. disease classification systems.

- Noted that ME and CFS patients could be potentially vulnerable to the current DSM 5 proposals because those proposals are highly subjective and difficult to quantify. Noted that retaining the CFS in the R-codes in the IDC 10 CM differentiates the U.S. from other countries but it renders CFS and ME patients more vulnerable to some of the DSM 5 proposals, notably chronic complex symptom disorder.

Dr. Klimas asked for clarification, and Dr. Jason said that in 2013 they would move from DSM 4 to DSM 5. As it stands they would be collapsing somatization disorder, undifferentiated somatoform disorder, hypochondriasis and some presentations of panic disorder into complex somatic symptom disorder. Dr. Klimas clarified that his concern was that the CFS ICD 9 codes would put the non post viral patients into this somatoform cluster. Dr. Jason indicated that this was so.

Dr. Klimas seconded the motion.

Mr. Krafchick agreed and stated that the ramifications of the classification would be disastrous for patients, because it would limit disability payments to two years. Dr. Jones clarified that for now the clock was ticking, however once the codes were released, they could be revised, it's just the implementation of the electronic system which is causing it to be locked at a particular point in time. While CFSAC has shared concerns with NCHS, there is an official process for engaging with them on their discussions regarding the codes. The US was interested in morbidity, in case claims. It is important that providers know how to best categorize things, and provide guidance on which codes to consider based on the science for the disease being evaluated.

Mr. Krafchick stated that the issue was that the criteria for the codes was etiology/trigger based. Dr. Jones clarified that it would still remain in the clinician's judgment, however if they could not identify where the trajectory developed toward CFS, then it would wind up in the R codes. Dr. Jones clarified also that the NCHS does not view the R category as a somatoform disorder. Mr. Krafchick and Dr. Snell indicated they understood this but it would still represent vulnerability for patients when classifying.

Dr. Jason restated his recommendation.

Dr. Marshall stated his concern that there was an attendant risk with this, but that they were between a rock and a hard place. He agreed CFS/ME being classified as a somatoform disorder was inappropriate, but at the same time that the recommendation says it's a complex multi-system disease, it categorizes it within a single nervous system disease silo. This might affect future research funding opportunities with people saying they don't fund neurological research. He expressed the view that they should advocate for classification in a multi-system disease category rather than putting it in a nervous system disease category for future, though this category did not exist now. It would be a good thing for patients short term, but it could be a long term risk.

Dr. Snell said that given the amount of current funding, this wasn't a risk. Dr. Marshall said that using reverse translational research as had been advocated during the meeting might increase the role of this categorization, and could be restrictive in funding.

Dr. Jones asked whether the recommendation being put forward was the same as the May 2010 recommendation, and Dr. Jason said that his was dramatically different. Mr. Krafchick underscored how the insurance companies use these ICD codes. If it was classified in something that could be psychiatric it will be psychiatric, so they can deny coverage.

Dr. Levine asked about co-morbid disorders and how these are weighted. Dr. Jones responded that she did not think that there was a weighting. It would get listed like a death certificate, a cause of death and then a secondary, sometimes a third. She stated it was the judgment of the clinician how it was listed.

Dr. Klimas expressed the view that coding was also problematic because clinicians code to get paid. There already exists a bias against coding CFS as CFS because the codes could not be used for billing. She stated that they would make a conscious decision not to code CFS as CFS. She indicated that

neurology was a fine place for it to be categorized, and at least this would assist people who may be looking for patient data, as it wouldn't be ignored.

Dr. Snell asked for a vote of all those in favor regarding Dr. Jason's motion. The motion passed unanimously.

Dr. Jones noted that she would share this recommendation with the NCHS but repeated that unless someone moved forward to intervene in the official processes in the public record it may not move forward or have an effect.

Dr. Jones noted that the next ICD meeting is September 14 – 15, 2011 with public comments due July 15. Noted this will be put on the CFSAC website. She noted she would check the rules to see if a member of the CFSAC or the Chair would be able to give public testimony at another advisory committee meeting. Mr. Krafchick said that if it were possible to send someone as a member of the committee, it would make a great deal of sense and be very important. Dr. Jones said they would figure out how this could happen. Ms. Holderman asked whether this notice, and any future notices where they might want to intervene, could be placed on the CDC website. She stated this cross listing would be useful.

Dr. Jones said that from her experience with the fast evolving HIV coding, there was a dialogue so that coding kept up. She expected there would be some connection, however not as comprehensive or active as that disease.

Dr. Mary Schweitzer, a member of the public, stated that the NCHS did come to CFSAC in 2005 and Dr. Reeves at the time was specific and said that CFS needed to be in R53 due to his own method of diagnosis. She suggested that this showed an obvious connection between the CFS side of CDC and NCHS at the time.

COMMITTEE DISCUSSION

Dr. Jason said they had some business from their sub-committee which would be helpful and suggested they hear from Dr. Houghton.

Dr. Houghton stated that all committee members acknowledged that the field needed more research funding in order to make progress. He said he thought it was important that CFSAC recommended that more funding was available for clinical and basic research on ME/CFS. He noted that the timing relative to the State of Knowledge Workshop was good and there was momentum. He thought that they should have a strong recommendation that there was more funding available for this disease from the NIH and, if possible, other bodies.

Dr. Houghton stated that he believed that the committee should make a strong recommendation that the NIH and other government bodies increase its funding for this disease at the level of clinical and basic research.

Dr. Marshall said they had been asking for money for a long time, and perhaps they should be more specific about what the committee would like them to fund. He noted that an RFA (Request for Application) sounded vague. Did they need to prioritize the research topics?

Dr. Snell noted that what was being said at the workshops was that researchers needed to collaborate more and a funding proposal that encouraged that sort of collaboration would be helpful. Dr. Marshall suggested being very specific in asking for something that might be less global but would have a defined purpose.

Dr. Jason said that conference grants could be applied for by committee members at any time. He noted by contrast the RFA can only be applied for when it is created by the people within NIH.

Dr. Klimas noted that historically there has been a successful RFA. She noted that the NIH had mentioned that they were not submitting enough applications. She acknowledged that this was a fair complaint as there were not enough investigators in the field. However she noted the previous RFA was $4 million which brought in more than 20 applications in a single round. She said it was a carefully-crafted pathogenesis RFA which brought good new people. She liked the idea of an RFA because it brought new ideas and people into the field.

Dr. Klimas recommended a potential RFA theme that came out of the meeting was the need to do networking, to use new technologies, to do translational work that lead to interventions.

Dr. Snell mentioned that they could attach the outcomes that came out of that workshop and assume that the NIH would come to the same conclusions that they did.

Dr. Houghton said that the funding should be commensurate with the disease burden in the country, one million sufferers. He thought that needed to be emphasized in the motion.

Ms. Holderman added to his comments saying it was not just the one million sufferers but the overall effect including the economic loss, a tax base loss, medical care, Medicare, Medicaid, all types of government entitlements. She emphasized that they needed to consider what it was costing the nation; the big picture.

Dr. Klimas asked Dr. Mangan if there was any possibility that they would ever be able to put together something like a MAPP (Multidisciplinary Approach to the Study of Chronic Pelvic Pain) for this illness. Dr. Mangan said he did not know the answer to that. He emphasized that creativity would be the key when they were under financial constraints. He noted that the MAPP program was fantastic and there was a lot to be learned from it.

Dr. Jones noted that Dr. Jordan Dimitrakov was sworn in during the morning. She asked him if he was one of the MAPP investigators. Dr. Dimitrakov confirmed that he was part of one of the institutions that was actually a sub-contractor to the MAPP program. He noted that one of the reasons that the MAPP initiative was very successful was that there was a built-in mechanism, a requirement in the RFA that it should be a collaborative approach. They had to specify which group they would collaborate with and that could potentially be built into the RFA..

Ms. Holderman asked Dr. Dimitrakov how much the funding was in that initiative. Dr. Dimitrakov said he believed it was $35 million at seven sites. Ms. Holderman stated that she understood the budget and

economic climate, but the disease had to be thought about in a new way, and we couldn't just put a band aid on it. She stated that the US was already paying for CFS in lost productivity, did they want to pay now or later, she suggested they pay now, keep scientists working, and get people well. She suggested they were justified and overdue in asking for a big number.

Dr. Marshall added that alongside the recommendation for funding there should be a requirement to interact in a multidisciplinary network, which would make people apply as a group, and would make the money go further. Dr. Marshall said they should add this degree of specificity to the recommendation, even as they recognize it is contingent on the NIH's final report.

Dr. Snell summarized that they wanted three things in a pithy recommendation: an RFA commensurate with the size of the problem and to emphasize inter-disciplinary and collaborative research. He asked would a MAPP RFA accomplish what they wanted with the inter-disciplinary research? Dr. Marshall clarified the difference between multi and interdisciplinary. Dr. Snell said that putting a number down would just beg the question of why that amount was requested, and the answer that that's what they were owed would not suffice.

Dr. Klimas suggested they didn't need to make reference to the MAPP project in the recommendation, this was just an example. The crucial part was that it involves networks, interdisciplinary research under an RFA, and that it leads to intervention. The funding needs to be commensurate, but again, need not reference the MAPP project.

Dr. Willis-Fillinger returned to the concept of reverse translation and this lead her to think about the CTSA (Clinical Translational Science Awards) where they engage in community based research, and wondered whether there would be resonance with reverse translational research at NIH. Dr. Mangan said that this was quite different from the MAPP model, he did not know a lot about this, but there were some examples of this sort of reverse translational work at NIH.

Dr. Dimitrakov said the MAPP project was about discovery of biomarkers and phenotyping , it isn't an effort to treat the disease, it was a response to 15 years of clinical trials without having well defined patients and subsets, which is a similar problem to CFS. The idea was to create the centers that recruit the patients and figure out using all available tools what the patients have. Treatment would follow. The RFA doesn't ask for a specific proposal or hypothesis.

Dr. Willis-Fillinger said that when they package the proposal they need to be careful about how they package reverse translational research as she wasn't sure what resonance there would be.

Dr. Dimitrakov was asked how they recruited the seven centers. He confirmed that they were not one of the seven centers but a competition was announced which said that there was an RFA and it said that you had to propose a concept for defining or phenotyping patients with chronic pelvic pain and at least one other overlapping condition. He noted that these overlapping conditions were listed in the RFA, and included CFS, fibromyalgia or chronic back pain. He said it was a concept proposal describing the kinds of patients and how they would be recruited. He said the centers were in their 4th year and were just recruiting patients

Dr. Jason said that as scientists many of the members of CFSAC were conservative in their actions but considering the crisis that they were facing he thought that perhaps it was time to be bolder and say plainly what could be done, not what is usually done.

Mr. Krafchick stressed that using the MAPP model would get at a number of areas in research that were not currently studied. Dr. Willis-Fillinger clarified the meaning of reverse translational research.

Dr. Klimas said that there was a pull in one direction to phenotyping, which was fairly far along despite poor funding, with many of the underlying reasons for persistence, and on the other hand was the body of knowledge from clinicians that experientially suggested what works. She stated the truth was they could do both of these things. She emphasized that they should consider organizing more data or knowledge networks so that important knowledge obtained would not be lost. She suggested using pockets of money designated under the Obama healthcare plan. She stated that if they identified great responses in CFS patients in clusters perhaps they could identify the reason for that great response. Dr. Dimitrakov agreed with this.

Dr. Levine stated that the issue was not much worked on CFS patients. Dr. Klimas suggested that there had been successes with individuals, and if there was enough good data about who was responsive and who wasn't, they could at least figure out how to treat some people. Dr Dimitrakov said that it was a good idea to have a single database to get those data sets together. Dr. Klimas agreed and said the timing was very good considering everything was going electronic right now. Dr. Levine said there needed to be better communication between clinicians and researchers.

Dr. Snell said there was a raft of suggestion for the recommendation, and they needed to identify the character of the RFA in preparation for the writing of the motion. Dr. Klimas said they could discuss this in the break. Dr. Mangan gave his opinions on how they should draft the initiative using different institutes.

Ms. Holderman asked how the MAPP initiative figure of $35 million was arrived upon. Dr. Mangan said that it was NIDDK institute (National Institute of Diabetes and Digestive and Kidney Diseases) driven thing, and the director probably had the final say, however three other institutes chipped in, this partnership was essential for a complex disease. Dr. Jones said that essentially money was pooled lead by one institute.

Dr. Snell said they would take an early break and put a workgroup together to figure out the wording of the recommendation.

BREAK

The Chronic Fatigue Syndrome Advisory Committee recessed for a ten minute break.

COMMITTEE DISCUSSION

Dr. Jason read the committee's recommendation:

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Given the enormous economic and human costs of ME/CFS CFSAC recommends an inter-agency funding effort including but not limited to NIH, CDC, CMS, AHRQ to adjust the gaps in knowledge identified at the April 2011 NIH State of Knowledge Workshop. Further CFSAC recommends that NIH or other appropriate agency issues an RFA financially commensurate with the magnitude of the problem for inter-disciplinary discovery and translational research involving inter-acting networks of clinical and basic science researchers. Areas to be examined should include the following: identification of patient subsets for detailed phenotyping and targeted therapeutic interventions, biomarker discovery, systems biology approaches and disability assessment.

Dr. Jones confirmed that the motion was seconded.

Dr. Snell confirmed that the motion was carried unanimously.

Public Comments - Afternoon Session

PUBLIC COMMENT

Rachel Smith (via telephone)

- Thanked the committee for allowing her to speak. Advised she was 27 years old and had been sick for over 20 years.
- Gave details of the few memories she had of a once healthy life and noted the changes after she became ill and how it affected her personal life and education.
- Gave details of how the lives of everyone around have progressed whereas her life has not moved. She related how when the illness affects the young it is particularly sad.
- Noted that everyone was living in a great country and if the people were creative and intelligent then she felt it was in their grasp to solve CFS/ME. Noted that they could and should promote more research, funding and hope for the future.

Charlotte von Salis

- Advised the committee that she had been sick since 1990.
- Noted that she and the patients present were only the tip of the iceberg.
- Described the many friends she had and their conditions and stated if they had been properly diagnosed and treated as having a neuroimmune disease using the CCC their lives may have been different.
- Noted the cost to the economy at $18 to $23 billion annually.
- Noted that representatives would be at the meeting the following day from the Social Security Administration (SSA) and the Department of Labor (DOL) and both agencies could help, SSA

could list the impairment in their blue book, shortening the process of getting disability insurance. DOL could use their advisors who work on improperly denied health and retirement benefits, and these could assist with disability plans.

- Noted issues with the CDC and their identification of CFS which it considers an enigma. Advised that outbreaks have been documented since 1934. The CDC does not have the exclusive authority to name disorders.
- Reviewed the studies and some of the issues along the long history of CFS. Discussed some of the research and funding issues. Stated that this research should not be ignored, delayed, or underfunded it should have the highest priority.
- Compared the government's fast reaction to the HIV AIDS to that of CFS. Stated public policy needs to change.
- Noted she had a petition signed by over 550 people stating that they did not want to be represented by the CFIDS organization.

Janine Militello (via telephone)

- Advised that her name was Janine Militello and she was 17 years old and was diagnosed with CFS and fibromyalgia four years ago.
- Told by her doctors that she needed to see a psychiatrist.
- Advised that after her diagnosis nothing changed and most doctors did not know how to help her and advised psychiatric help.
- Advised that many people recommended doctors but they refused to see her because she was not yet 18 years old. Noted many doctors had different ideas and she had many symptoms.
- Described how this adversely affected her education and social life.
- Described how she wanted her future to be and her dreams of a medical career.

Thomas Hennessy (via telephone)

- Greeted CFSAC and thanked Dr. Jones and the ME accountability committee for scheduling the meeting around the 19th annual ME awareness day.
- Advised that he wanted to talk about funding. Discussed the NIH funding to other causes such as anthrax that had been getting over $100 million a year for the past decade. Noted that only about a dozen people have been made sick by anthrax in the past ten years.
- Asked for $250 million to be put into this area.
- Asked that they adopt the Canadian Consensus Criteria definition today and discontinue every other definition.

- Demanded that NIH funding be increased to $250 million for FY2012. Mentioned a petition signed by almost 10,000 to this effect.
- Asked them to get clinicians and researchers who had seen 1,000 patients in a clinical setting and give them a stipend of $250,000 to rewrite the CDC website.
- Stated they should fund proper replication trials for XMRV. Asked that they fast-track ampligen.
- Noted that the Pentagon should declare the disease a national emergency as there were 285,000 sick Gulf War veterans.
- Fund the centers of excellence and staff them with expertise and experience in the field.
- Asked that the CDC start to hire competent staff immediately.
- Stated that a class action lawsuit should be pursued against insurance companies who he claims are denying care through fraud and bribery.

Mary M. Schweitzer

- Asked why Ampligen had not been fast-tracked. It has been available for over 20 years, and she had been on it for 9 years. There were no alternatives.
- Asked why NIH spent less than 1 percent on CFS compared to what they spend on multiple sclerosis (MS).
- Asked why 850,000 of the 1 million Americans with her disease were left undiagnosed 25 years later.
- Said that someone is sending the message that CFS was not a serious disease and she felt that that was mainly the CDC.
- The CDC indicated they were working on biomedical research on CFS, she stated they were not, and all they really wanted the CDC to do was to put forth the latest reliable biomedical information on CFS.
- Discussed the problems with the CDC website including inadequate data information. Noted a lot of information was available and it was not the mysterious disease they made it out to be. Noted there was no information about ampligen and testing.
- Asked why there was so much disinformation on the CDC website. Noted that there was too much influence from British psychiatrists, (including Dr. Peter White) who she alleged were associated with insurance companies.

Robert Miller

- Noted that he was worth more than $3.64, the amount he understood was spent on funding per patient per year. He put that amount of money on the table.
- Greeted the committee members, patients and audience. Stated he was Robert Miller, a ME/CFS patient of 25 years from Reno, Nevada.
- Thanked the CFSAC for listening and for their continued efforts. Thanked Dr. Jones and her staff for guiding the meeting.
- Thanked President Barack Obama for promising his wife at a recent town hall meeting that he would talk with the NIH and see what they could do to increase the scientific research on ME/CFS.
- Noted that his wife was able to contrast the multi-billion dollar cost to the U.S. taxpayers for disability, Medicare, and lost tax revenues with the paltry $6 million the NIH is spending annually for research that affects 4 million patients.
- Stated that President Obama's response to his wife referenced faith; he stated that God had given us intelligence to figure things out and to make lives better. Stated that the president's response gave him faith again.
- Noted he had faith in science to solve these problems and science needed to be funded.
- Thanked Dr. Mangan for the State of the Knowledge Workshop and all his work.
- Compared the number of centers of excellence and funding for ME/CFS with other diseases. Noted there was no center of excellence for ME/CFS. Stated they should ask for $100 million annually by 2014.

Kathleen Manganaro

- Greeted the committee and stated that her name was Kathleen Manganaro and she had had ME/CFS since 1984.
- Stated that she wanted to discuss the role that bio-toxins and molds had played in her illness. Noted that if doctors had known about the mold connection to her CFS there would be no question that a great part of her pain could have been prevented.
- Noted that in 1983 she was healthy. Went back to work and in her office one of the buildings had a roof leak. Noted that it had water damage and mold. Noted that the building made her feel sick and gave her a variety of classic CFS symptoms that got worse over time. In 1985 she saw an integrative physician who helped her regain some health with an anti-mold protocol.
- Noted that six young teachers developed different cancers and died within a short period of time of diagnosis in that building.
- Related how the disease affected her personal health, pregnancy and her twin daughters died shortly after birth.

- Noted that in 1992 she left the building and from 1992 to 2003 her health was stable. Noted that in 2003 she was assigned to a basement room again and her symptoms returned. Noted that by May 2007 she had to stop working.
- Described the treatment she received which caused a major heart attack after thyroid medication.
- Urged doctors to consider if their CFS patients might be getting exposure to toxic mold and to encourage them to reduce those exposures.

Dr. Joan Grobstein

- Greeted the committee and stated that she was a physician.
- Stated that they needed to prioritize and establish an agenda for future initiatives.
- Noted that in the absence of leadership from the NIH, the CDC and the CFSAC or any other agency in the Department of Health and Human Services stated she would make suggestions that should be implemented within the next six months.
- Discussed the case of a young patient who was diagnosed with ME/CFS at age nine and worsened at age 15. He died suddenly at age 23.
- Stated that an autopsy was done and the pathologist said that his heart tissue was quote, "loaded with viruses, inflammation and fibrosis." Noted the University of Wisconsin lost the heart tissue blocks and the viruses were never identified. Asked what did they think the case said about priorities and an agenda for future initiatives.
- Stated that ME/CFS is likely transmitted within families and establishing the mode of transmission should be a priority. Noted that as far as she knew the CDC had never investigated family clusters or geographic clusters for more than a decade.
- Remarked that to enable physicians to report the disease there must be a definition and stated that the best definition available was the Canadian Consensus Criteria definition. Stated that it should be adopted now and disseminated to all physicians.
- Stated that epidemiologic studies should be started immediately.
- Noted that the CDC should contact observational, longitudinal studies of Canadian Consensus-defined ME/CFS.
- Stressed that it was urgent that associated viruses be identified and treated if possible. Stated that new anti-virals would need to be developed.
- Gave an opinion that medical schools do not take ME/CFS seriously. Stated that the NIH should convene a meeting of medical school leaders to educate them about the seriousness of the disease.

- Noted that treatments for ME/CFS exist and expert clinicians were using anti-virals, dietary supplements, sleep medications and other treatments some of which are successful. Stated that the NIH should convene a meeting with clinicians to formulate guidelines for diagnostic testing and treatment.
- Reviewed the inadequacies of the CDC website.

Nancy Richardson

- Greeted the committee and said she was Nancy Richardson and she was the education and outreach director for Hemispherx Biopharma. Advised she wanted to give an update to the committee about their progress. Noted that working with the Whittemore Peterson Institute, Hemispherx had monitored blood from patients.
- Noted that the results of this study suggested that XMRV antibody positive cohort had a greater relative percent of patients showing significantly increased exercise duration with Ampligen treatment compared to placebo.
- Noted they are expanding their protocol to include monitoring for XMRV. They are opening new clinical sites, and are expanding virus signatures they are evaluating. They have partnered with Chronix to this end.
- They are assessing whether there may be a unique serum DNA sequence in the blood of CFS patients, and will be presenting on this in coming months.
- Noted Hemispherx conducted a clinical investigators meeting in Florida, and detailed discussion and presentations made there. Highlighted a Wall Street Journal article that came out of this meeting.

COMMITTEE DISCUSSION AND PLANS FOR DAY 2

Dr. Snell indicated that there was some leftover discussion from the lunchtime meeting. He stated that one topic was a request to the CDC that they consider commissioning a group from their panel of experts to review the website with the possibility of making appropriate changes.

Dr. Jason suggested maybe putting it as a motion, and suggested rather than asking them to continue to refine it, instead have a group of people look at it who would report back to CFSAC. Dr Snell asked if the recommendation could be to the Secretary to request the CDC as opposed to a direct request from the committee to the CDC. Dr. Jason confirmed it was for the Secretary to appoint a group.

Dr. Klimas stated she would argue against anything that developed into a long process. She thought that the CDC might first review and edit the website for incorrect or outdated information, and this could occur quickly.

Dr. Miller stated that even working with a small team of three they could review the site and make recommendations. He stated that the CDC did not want anything on the website that would be intentionally derogatory to any patient or patient care. He recommended leaving it as a task for the committee.

Dr. Klimas stated that the whole CDC website was not incorrect, only elements of it. She confirmed that the NIH website also needed to be updated. Dr. Klimas' concern was how these sites were used by insurance companies and therefore affecting patient care. She also added that if the CDC removed sections from their site as inappropriate that they state why it was removed again for the benefit of insurance companies.

Dr. Jason asked whether there could be patient representation on the group looking over the website. Dr. Snell advised that Dr. Miller had recommended Dr. Klimas, Ms. Holderman and Dr. Cook for the panel to review the CDC website. He asked if they would be willing to engage. They all confirmed they would. Dr. Jason said that patients could be on if they were a good sounding board, but she expected she would hear from them.

Barbara Soliday, a member of the public, suggested that they do it tonight, since it was only a couple paragraphs. Klimas said that indeed they could put together a couple paragraphs quickly, although this shouldn't be the whole project. Dr. Snell agreed and said there should be a more systematic approach.

Marly Silverman, a member of the public, stressed the disability approval issues that come up with this, and those are the most significant issues that come up. Dr. Snell indicated that it would be helpful for her to pass on any edits she would suggest.

Another member of the public, Meghan Shannon said if they were going to make the changes, they should do it all the way, and not do it too hastily. This would entail taking the website down, updating it, and then informing everyone that this information has changed; there had to be an educational component.

Dr. Snell indicated that the idea would be that the most glaring issues would be addressed, then a more thoroughgoing approach would be taken.

Dr. Miller indicated that any appropriate recommendations would be considered and implemented, and he didn't know of any significant roadblocks to editing the website. He agreed that the committee and its members sounded good. Dr. Snell said he would make the recommendations public.

A member of the public said that any substantive review of the website shouldn't just deal with insurance and clinicians, but also take into account new patients who were just learning about the disease, and how crucial it was for them to have a good understanding of what they were experiencing and some idea of opportunities for treatment. Dr. Snell assured everyone that the committee was well aware of the significance of the CDC website, and were very happy to have the CDC's ear on this. Dr. Jason indicated that there were other websites as well that would benefit from the same analysis, and stated that inviting patient involvement in every process was difficult, but ultimately rewarding.

Dr. Mangan indicated that if they had any feedback on the NIH website, they'd welcome it. Dr. Klimas indicated that the NIH website was an improvement but there was potential there, for instance a toolkit for researchers in the field which would provide consistency.

Dr. Snell discussed the sorts of measures that everyone should be taking as a matter of course when doing research or treating patients. Confirmed that this came up in both working groups. He said it concerned getting a better-characterized group of patients so that when they're selected for research studies they know what they would be getting and secondly, when successful treatments are seen they can make some assertions about why they might be working.

Dr. Jason indicated that every paper on the subject should define the cohort so everyone was aware of who was in the sample. He said their sub-committee had difficulties defining the boundaries of what would be useful for the field.

Dr. Klimas advised that her sub-committee was brainstorming about how one might use agency resources to expand patient access to care. Also she noted in developing such a platform one could use a basic set of case report forms and you would then be able to do some work that would allow them to sub-group patients and look at responses. She also discussed the identification of physicians in the field that had identified the disease so that they could be further educated. They would then be a valuable primary resource in the field. Mr. Krafchick said that this sort of model was very exciting, and doable.

Dr. Jones said that the *ex officios* had discussed tasking people on answering a question, or working on a particular concrete issue. Was there a willingness to work with *ex officios* to formulate a work plan cooperatively? Dr. Klimas said that now they had a better understanding of what was possible, there was enthusiasm about what could be done, but they'd probably need to draw in people from outside the committee to do this. Dr. Snell echoed Dr. Klimas' appreciation for how open the lines of communication had become.

Dr. Jason said that often the committee came up with great ideas, but leave with no concrete next steps. They need to set a couple focused things and accomplish them.

Dr. Jones confirmed that Dr. Howard Koh would be there the next day. He could not be in attendance the first day because of a scheduling conflict. She reviewed the agenda for day two.

ADJOURNMENT

The Chronic Fatigue Syndrome Advisory Committee adjourned for the day at 5:00 p.m. The committee will reconvene tomorrow, Wednesday May 11, 2011 at 9:00 a.m.

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