Spring 2012 Meeting
of
The Chronic Fatigue Syndrome Advisory Committee
U.S. Department of Health and Human Services

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

Thursday, June 14, 2012 – 9:00 am to 5:00 pm

Voting Members

Chair
Gailen Marshall, Jr., M.D., Ph.D.
Jackson, MS
Term: 04/10/10 to 04/10/14

Dane B. Cook, Ph.D.
Madison, WI
Term: 04/10/10 to 04/10/14

Jordan D. Dimitrakoff, M.D., Ph.D.
Boston, MA
Term: 04/10/11 to 04/10/15

Eileen Holderman
Galveston, TX
Term: 04/10/10 to 04/10/14

Susan M. Levine, M.D.
New York, NY
Term: 05/10/10 to 05/10/14

Ann Vincent, M.D.
Rochester, MN
Term: 04/10/11 to 04/10/15

Adrian M. Casillas, M.D.
Shreveport, LA
Term: 06/13/12 to 06/13/16

Lisa Corbin, M.D.
Denver, CO
Term: 06/13/12 to 06/13/16

Mary Ann Fletcher, Ph.D.
Miami, FL
Term: 06/13/12 to 06/13/16

Steven P. Krafchick, M.P.H., J.D.
Seattle, WA
Term: 07/01/10 to 07/01/14

Jacqueline E. Rose, M.D.
Columbia, MD
Term: 06/13/12 to 06/13/16

Ex Officio Members

National Institutes of Health

Susan Maier, M.D., *Primary*
Senior Advisor
Office of Research on Women's Health
Office of the Director

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

Social Security Administration

Cheryl A. Williams, *Primary*
Office Director
Office of Medical Listings Improvement

Amanda Wulf, *Alternate*
Acting Deputy Director
Office of Medical Listings Improvement

Agency for Healthcare Research And Quality

Beth A. Collins Sharp, Ph.D., R.N.
Senior Advisor for Women's Health and Gender Research

Centers for Medicare and Medicaid Services

Alaine Perry, M.P.H.
Senior Advisor
Center for Strategic Planning
Strategic Planning Group
CMS Center for Strategic Planning

Centers for Disease Control and Prevention

Ermias Belay, M.D.
Associate Director for Epidemiologic Science
Division of High-Consequence Pathogens

Health Resources and Services Administration

Deborah Willis-Fillinger, M.D.
Senior Medical Advisor
HIV/AIDS Bureau

Food and Drug Administration

Theresa Michele, M.D., *Primary*
Medical Officer Team Leader
Center for Drug Evaluation and Research

Keith Hull, M.D., Ph.D., *Alternate*
Center for Drug Evaluation and Research
Division of Pulmonary, Allergy, and Rheumatology Products

Designated Federal Officer

Nancy C. Lee, M.D.
Deputy Assistant Secretary for Health-Women's Health

Alternate Designated Federal Officer

Martha D. Bond
Senior Public Health Advisor
Office on Women's Health

Agenda
CFSAC Spring 2012 Meeting
Thursday, June 14, 2012

9:00 am	Call to Order Opening Remarks	pg 4	Nancy C. Lee, M.D. *Designated Federal Official*
	Roll Call, Housekeeping		
9:15 am	Agency Updates: AHRQ, NIH, HRSA, CMS	pg 5	Ex Officio Members
10:15 am	Funding and Other Support	pg 17	Ex Officio Members
11:15 am	Break	pg 26	
11:30 am	Public Comment	pg 56	Public
12:15 pm	Lunch Break	pg 26	Subcommittee Members
1:15 pm	ME/CFS Organizations	Pg 26	Committee Members Panel Discussion ME/CFS Organizations
2:15 pm	Break	pg 36	
2:30 pm	ME/CFS Case Definition – A Path Forward to Consensus	Pg 37	Committee Members
3:30 pm	Committee Discussion: Finalize Recommendations	pg 48	Committee Members
5:00 pm	Adjourn	Pg 55	

Thursday, June 14, 2012

The following document contains highlights of the Chronic Fatigue Syndrome Advisory Committee (CFSAC) Meeting held on June 14, 2012. Access a videocast of complete meeting proceedings at http://www.hhs.gov/advcomdfs/meetings.

Call to Order/Opening Remarks

Dr. Nancy Lee

- Welcomed meeting attendees.
- Noted that people were still working their way to the meeting room through the security system in the HHS lobby.
- Thanked Dr. Marshall for his leadership and reminded attendees that he was traveling to a meeting in Geneva.
- Noted that the fourth new CFSAC member—Dr. Lisa Corbin—was making her way from Reagan National Airport (Washington, D.C.) after a red-eye flight from Denver and would be sworn in when she arrives.

Roll Call

Dr. Lee conducted roll call by requesting that CFSAC members call off their names.

Voting members present:

Adrian Casillas
Mary Ann Fletcher
Jordan Dimitrakoff
Eileen Holderman
Dane Cook
Susan Levine
Ann Vincent
Jacqueline Rose
Steve Krafchick

Absent: Drs. Marshall and Corbin (see opening remarks)

Ex Officio members present:

Beth Collins Sharp, Agency for Healthcare Research and Quality (AHRQ)
Deborah Willis-Fillinger, Health Resources and Services Administration (HRSA)
Theresa Michele, Food and Drug Administration (FDA)
Ermias Belay, Centers for Disease Control and Prevention (CDC)
Susan Maier, National Institutes of Health
Alaine Perry, Centers for Medicare and Medicaid Services

Absent: Social Security Administration representative

Also present:

Nancy Lee, Designated Federal Officer (DFO)
Marty Bond, Alternate DFO

Housekeeping

Dr. Nancy Lee

- Reminded participants to press the red button to activate microphones to be heard for purposes of meeting minutes, recording, live webcasting, and audio streaming via phone.
- Expressed hope that the live video streaming and audio hookup worked the previous day.
- Expressed gratitude for the technical accommodations, given the budgetary situation in Washington, D.C. Noted that she does not know how long these opportunities will last. She explained that CFSAC could no longer afford its previous contractor and that the current contractor is in-house.
- Asked CFSAC members if they had any comments before proceeding to agency updates.

Mr. Krafchick: I'd like to resurrect the motion from yesterday on the use of the primer and modify it slightly.

Dr. Lee: Can we do that this afternoon during the discussion or do you want to do it now?

Dr. Levine: Steve, I would wait. There might be a fair amount of discussion and we don't want to hold up the speakers.

Mr. Krafchick: Fair enough.

Agency Updates

Agency for Healthcare Research and Quality
Beth Collins Sharp, Ph.D., R.N., *Senior Advisor for Women's Health and Gender Research*

- Explained that her presentation would be relatively short because there are not a lot of new items to report since the November CFSAC meeting.

- Noted that she will have more to tell CFSAC members during the funding opportunities discussion.

- Explained that AHRQ is one of the smallest agencies, if not the smallest agency, within HHS. AHRQ is a research agency, not a regulatory agency. AHRQ focuses on health*care* research, not *health* research.

- The agency's research portfolios do not focus on specific disease entities, but rather on health services research such as health information technology, patient-centered outcomes, patient safety, primary care and prevention, value, and innovations.

- AHRQ has a small grants program that is investigator-initiated. This will be a topic for the funding opportunities discussion.

- AHRQ has a number of contracts, one of which is the Medical Expenditure Panel Survey. As the name implies, this is an annual survey of medical expenditures. It is a generalized survey but it is well-respected and used quite a bit by Congress and other stakeholders.

- Just prior to the November CFSAC meeting, AHRQ put out a statistical brief on healthcare use and expenditures for pain conditions among women. The brief was a pooling of data around a number of pain conditions, including CFS. Some of the others were FM, TMJ (temporomandibular joint disorder), vulvodynia, and endometriosis. The brief covered a whole gamut of conditions.

- The investigator who did the brief and the statistician were asked if they could pull out the CFS patients to look at those individually. The number was just too few, even though they tried to be creative and pool data across about 10 years. They still were unable to pool enough data to do any meaningful analysis. Dr. Collins Sharp expressed disappointment at this outcome. She said that she did not provide this example to add to CFSAC members' frustration, but to show that this is one of AHRQ's challenges. "I just wanted to give this real- life example from our perspective of how it's frustrating on this end as well," she concluded. "There are attempts to do these sorts of analysis."

National Institutes of Health
Susan Maier, M.D.

- NIH turns research discovery into health and applications. The agency is made up of 27 institutes and centers. Each has a specific research agenda. Sometimes the agenda focuses on a specific disease; other times it focuses on a particular function such as review.

- NIH leadership plays a very active role in shaping the research agendas for the entire NIH, along with stakeholder input.

Trans-NIH ME/CFS Working Group

- The Trans-NIH ME/CFS Working Group (WG) is the vehicle for research and activities related to ME/CFS across NIH. The WG is located in the Office of Research on Women's Health. This is in the Division of Program Coordination Planning and Strategic Initiatives within the Office of the Director at NIH. We are not within an institute. We are within the Office of the Director.

- Membership on the WG includes representatives from 16 NIH institutes, centers, and offices. The WG recently recruited membership from the new Center for Advancement in Translational Sciences (NCATS).

- I am the chair of the WG as well as serving as the CFSAC NIH *ex officio*.

- The duties of the WG are wide-ranging:

    - Look at cross-cutting areas of research in ME/CFS.
    - Try to identify and match resources that are needed by investigators with opportunities that are available at NIH and across other agencies.
    - Disseminate information about ME/CFS research findings through a public website and a listserv.
    - Communicate new and ongoing research activities to the NIH leadership directly and to HHS leadership through CFSAC.

- Hold monthly meetings, update the website, provide information to potential applicants, and seek out new investigators to the field. They may not be doing research on ME/CFS but they might be doing something in a very similar field or a very similar area. WG tries to leverage these investigators' expertise to try to advance ME/CFS research.
- Develop plans for moving the field forward.

Accomplishments

The WG has several accomplishments. I have only been in this position since January. I think that we have done quite a bit and I hope to do quite a bit more:

- Developed a dedicated internal website for communication, document review, and sharing ideas across all the institutes and centers.

- Hosted guest speakers who have expertise in areas that interest WG. An example is an intramural researcher from the Nursing Institute who talked about his research on fatigue and the genomic aspect of identifying various subgroups of fatigued individuals in cancer patients. His next project will be with CFS patients. WG also had a speaker talk about strategic planning—how to develop, evaluate, and track progress on strategic planning. An important aspect of moving things forward is being able to develop a plan and evaluate how well that plan is working.

- Developed a list of priorities from the State of the Knowledge Workshop on ME/CFS. Next we will turn those recommendations into actionable items using an action matrix. WG will try to identify the short-term, low-cost things that we can do as well as moving some of the recommendations into the long-term, high-cost area. This is one way to move forward—get all those recommendations into an action matrix.

- The Center for Scientific Review agreed to change the name of the review panel dedicated to reviewing applications on CFS. "ME/CFS" will replace the "CFS" in the panel's name.

Future Activities and Plans

- Collaborate with other trans-NIH working groups. An example is the trans-NIH Chronic Overlapping Pain Conditions Working Group, a relatively new WG. It brings together individuals from across NIH with an interest in chronic overlapping pain conditions. The group is holding a conference in August that is open to the public. Information about the conference and how to register will be on the ME/CFS WG listserv when available. The ME/CFS WG is also working with the Pain Consortium and recently awarded 11 contracts to develop and disseminate educational materials for health professionals on all aspects of pain, including pain treatment and pain management. There are a wide range of activities that are ongoing in these centers, including educational materials for nurses, pharmacists, physicians, and dental practitioners. The ME/CFS WG wants to leverage the resources and expertise from others to advance its own mission.

- Develop the means for documenting and storing consistent, well-defined, and reliable research outcomes using current tools and resources.

- Identify methods to engage multiple ME/CFS researchers to collaborate on projects with defined outcomes.

Grants Funded by NIH: ME/CFS

NIH spent $6.3 million dollars in fiscal year 2011 funding ME/CFS research grants. The project examples on my presentation slide are not my favorites and they are not the only ones. They do demonstrate that NIH funds a variety of activities.

For example, if you look at the first grant—Efficacy of Home-Based Self Management for Chronic Fatigue—you see that it is labeled "R42." The R42 mechanism is a small business technology transfer grant. These grants support in-depth development of R&D ideas whose feasibility has been established and that will result in commercial products—things people can use.

The second grant from the bottom is an F30 mechanism. This is an individual pre-doctoral fellowship for M.D. or Ph.D. candidates used to train future physician researchers. We're training the next generation of researchers and if they are doing projects on ME/CFS, then it is very likely they will continue in this field. We think this is an important way to go.

Clinical Trials: ME/CFS

Clinical research relies on human subjects. Everyone can make a difference.

The ClinicalTrials.gov website allows a search of clinical trials in any disease area. You can search by geographical location. I used the search term "chronic fatigue syndrome" and found 37 NIH studies that are either open, or open and recruiting. I refer to the slide examples as drug and non-drug interventions that are being tested in trials. My FDA colleagues might disagree with that classification, but as a biologist, it works for me.

NIH Funding Opportunities: ME/CFS

This will be discussed during the funding opportunities session, but I wanted to give you a flavor of what happens:

- The NIH funds through grants or contracts.
- There are investigator-initiated applications, or solicited or targeted applications. Seventy percent of the applications NIH receives are investigator-initiated. I want to stress that even though we put out a solicited or targeted application or a targeted request for applications and there are set-aside funds attached to it, that doesn't meant that it will be awarded. All applications that come in to NIH have to be reviewed. It's a competition for the best science.

<u>First funding slide</u>: Parent announcements are those that investigators can use to submit their applications. These are the application notices for the investigator-initiated grants.

<u>Second funding slide</u>: These are solicited—or very targeted—announcements. The slide includes Pas, which are program announcements, and RFAs, which are requests for applications.

<u>Third funding slide</u>: These are solicited funding opportunities for ME/CFS that includes our very favorites up at the top. Those are PARs, which are program announcements with a specific review panel attached to then.

<u>Fourth and fifth funding slides</u>: These are opportunities listed under "fatigue" and "pain." I think it is important to look for opportunities beyond the letters ME/CFS in an era of flat budgets, limited funds, and limited people resources. This is what we're going to have to do as an approach to get the maximum amount of research done with limited funds.

Other Opportunities to Advance ME/CFS Research

The National Center for Advancing Translation Sciences (NCATS)

Drug Rescue and Repurposing

NCATS' mission is to catalyze the generation of innovative methods and technologies that enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions. This is the newest center to be added to NIH. It has a very specific program announcement coming out.

The center has a division that deals with drug rescue and repurposing. The repurposing program takes drugs that have been used for other disorders and diseases in the past and sees if they are applicable to different diseases and disease categories. The drug rescue program is for chemicals that have been abandoned during development by a drug company because they are not going to work for the purpose they were intended. NIH has gone into agreement with Pfizer, Lilly, and Roche to allow investigators to rescue those drugs and allow them to be used in clinical trials. I think this is a fantastic opportunity. I'm not sure what will come of it, but I think it is an opportunity worth pursuing.

Clinical Translational Science Awards (CTSAs)

These are very large awards. They provide the critical infrastructure and support needed to advance clinical translational science. There are CTSAs across the country. They are always looking for partners; always looking to bring in new people. I think if the infrastructure is what's needed by individual investigators who want to work on ME/CFS, this is an opportunity for them to be brought into that fold and have access to those resources.

NIH Clinical Center

The NIH Clinical Center (CC) is the nation's largest hospital devoted entirely to clinical research. It has a very broad mission statement that includes:

- Investigating the pathogenesis of disease
- Developing state-of-the-art diagnostic, preventative, and therapeutic interventions
- Conducting human clinical trials with an emphasis on rare diseases and diseases of high public impact

A thousand clinical research studies are underway at the clinical center. [Dr. Maier presented a slide showing some search results for currently active clinical center protocols related to CFS.] These are opportunities for the clinical center to collaborate. It's a new model that has just been adopted by NIH. It's intended to open up the clinical center to all researchers to come in with a defined protocol and perform research.

The Undiagnosed Diseases Program

This program is still available and requires an application to get in.

[Dr. Maier concluded with a slide showing several definitions for the word "opportunity." She noted that her favorite definition is "a prospect for success and this is what NIH is looking for—the opportunity to work together for a prospect for success." Dr. Maier's slide show also includes a listing of websites for items to which she referred in her presentation.]

Health Resources and Services Administration
Deborah Willis-Fillinger, M.D., *Senior Medical Advisor, HIV/AIDS Bureau*

HRSA is the HHS agency that focuses on access to healthcare services. We focus on services to vulnerable and underserved populations. Most of the programs that we fund are not disease-specific, except for HIV/AIDS. We primarily focus on support for services and for infrastructure for healthcare services. For example, we have five bureaus. [Dr. Willis-Fillinger described four]:

- Bureau of Health Professions – Focuses on health professions, education, and training.
- A bureau that focuses on HIV/AIDS education, training, and resources for healthcare services.
- Maternal and Child Health Bureau – Focuses on support for women, children, and families.
- A bureau that focuses on primary health care services infrastructure and direct care services. The community health center program that has been mentioned in the past falls under this bureau. About 16 of these centers participated in Project Echo, which helped providers in communities learn how to adequately serve their patients with hepatitis C. That program has expanded to include HIV and other diseases as well.

HRSA Activities Since November 2011 CFSAC Meeting

- We were excited to see the CME that was developed by the CDC. HRSA has begun distributing that CME to the healthcare professionals associated with our programs. HRSA has a number of listservs, newsletters, and other ways to communicate with its grantees and healthcare providers who provide direct care services. That CME, along with an explanation of CFS, is being distributed throughout the community health center network, which serves between 20 and 60 million people a day. It's very important for us to get information about the CME into the hands of providers who care for patients.

- Another example is a program that we call Family to Family (F2F). I have mentioned it before. There are 51 F2F networks funded across the country. They have been in existence since 2005. The most recent budget is about $4.9 million dollars. The centers provide information to families to help them make healthcare decisions that are right for their children. The centers are staffed by trained family leaders who have children with special healthcare needs. The centers help families navigate federal, state, and local public and private healthcare infrastructure systems with a focus on advocating to get families the services they need.

- As I listened to the presentation yesterday by the Department of Education on the technical assistance programs, I sent a quick email to my colleague who runs the F2F program and asked if any of those grantees might be the same. She said absolutely yes. So some of the same entities that get funded by the Department of Education to provide technical assistance regarding school access also get support from the F2F program. I thought that was exciting, especially since I know we sent out our explanations of CFS/ME to these locations just a few weeks ago.

Centers for Medicare and Medicaid Services
Alaine Perry, M.P.H., *Senior Advisor for Disability and Special Need Population*

- Ms. Perry welcomed new CFSAC members and said she looks forward to working with them. She also thanked members of the public who traveled to the meeting and who will testify.

- She noted that she passed out a list of websites so that people would not have to struggle to write them down during her presentation. She added that the list would also be posted as part of the CFSAC meeting record.

- She described CMS as the agency that administers the Medicare program (which provides healthcare for the elderly and persons with disabilities) and the federal portions of Medicaid and Children's Health Insurance Program, both of which are joint state/federal programs. Overall, 100 million Americans receive health insurance through a CMS program.

- People with CFS may be eligible for Medicare or Medicaid based on age, disability, low income, or some combination. For example:

    - If an individual with CFS becomes entitled to Social Security disability benefits after the 24-month waiting period, the person would then also become eligible for Medicare.
    - If an individual becomes entitled to Supplemental Security Income (SSI) (which is for people with limited income due to a disability), in most cases that person would also become entitled to Medicaid.
    - CMS could cover people with CFS who are eligible for Medicare because they are elderly or who are eligible for Medicaid because they are low income.

With passage of the Affordable Care Act (ACA), CMS gained a few additional functions:

- The act created the CMS Innovation Center, which is charged with testing and developing new models of healthcare service delivery and payment. Ms. Perry said she would discuss the center during the funding opportunity session.

- CMS is now in charge of implementing a number of portions of the ACA that deal with the private health insurance market and the expansion of health insurance options. These include:

    - Working with the states to develop the new health insurance exchanges, due to go into effect in 2014
    - Overseeing new consumer protections in the private health insurance market
    - Providing consumers with better access to information about their health insurance options and their rights and consumer protections

- At the last CFSAC meeting, members discussed coverage denials for CFS services and treatment. Dr. Lee asked if there was any role that CMS could play in addressing this issue. Ms. Perry discovered that some of the new protections and programs under the ACA could potentially be helpful:

    - The healthcare.gov website was created to provide all Americans with information about insurance options. The website improved transparency and the ability of consumers to make informed choices about their health insurance. It's very accessible. The site has nice search functions, allowing consumer to search state-by-state for the different health insurance options available. Consumers can enter characteristics about themselves to search. If someone is low income and has a disability, for example, the site will bring up different options to explore. The site also has detailed plain-English explanations of new consumer protections under ACA.

    - An important consumer protection relevant to the CFS field is the new appeal rights regarding claims denials. The new rules apply to healthcare plans created after March 23, 2010, when the ACA became law. These appeal rights apply to health insurance plans, not to private disability insurance plans. The rights include standards on how plans must handle internal appeals.

The rules also provide the right to external review by an independent review organization. If a consumer goes through an appeals process within his or her plan and does not get satisfactory results, the person has the right to go to an external body that has no financial ties to his or her plan.

The new rules exclude what are referred to as grandfathered plans, which are health plans that were in existence before the law. It gets complicated because how much can a plan change and still be the same plan? If a plan was in existence before the law but changes significantly, it may no longer be considered the same plan and it may lose its grandfathered status. The website includes more details. The ACA requires all insurers to provide consumers with information about whether or not a plan is grandfathered.

- The ACA also created Consumer Assistance Programs (CAPs), which are state-level programs funded by CMS through grants. CAPs can help consumers to find healthcare coverage, file an appeal against a health plan, and learn about their rights. CAPS are also required to track complaints. CAPs can be state agencies or local nonprofits that are contracted by the state. They are not currently in every state. The HHS Secretary recently announced a new round of funding for CAPs, so hopefully there will be more. A consumer can search-by-state on healthcare.gov for CAP locations' contact information. The website also lists other options if there is not a consumer assistance program in a consumer's state.

Next Steps

- CMS is interested in feedback as it moves forward. The agency is in a period of transition with implementing the ACA and would like to have feedback on how these new protections and appeals rights are working for consumers.

- CMS does not have an official structure right now for compiling complaints that consumers bring at the federal level, said Ms Perry. She welcomed any help from CFSAC or the advocacy groups in compiling complaints and concerns raised by people with CFS about claims denials.

- She asked meeting attendees to spread the word about the website and consumer assistance programs, especially for getting help with filing appeals of denials. She expressed hope that the consumer protections work for people and again encouraged compilation of a record to assist CMS in seeing if patterns develop. "Are there concerns? Are there places where there are gaps that need to be filled? Knowing these things would be extremely helpful," she said.

- She also encouraged consumers to inform her about issues with Medicare coverage for people with CFS, treatments that Medicare does not cover, or situations where people are not getting claims approved.

- Ms. Perry noted that CMS recently announced a new data initiative. The agency has huge amounts of claims data from Medicare and some from Medicaid, although that situation is more complicated because it's a joint federal/state program. This claims data is potentially a valuable information source for researchers. CMS is working now on making development, management, and dissemination of that information a core function of the agency. The initiative goes beyond recordkeeping for claims to consider that data a national resource for improving healthcare quality and allowing researchers to look into all kinds of things. Ms. Perry directed people who are interested in the initiative to log onto the web address available from her handout.

- Ms Perry concluded that her door is open to discussing questions or concerns.

Dr. Lee noted that a big part of her job is pushing out the good news about the ACA, which she described as a very complicated 800-page piece of legislation. She said the ACA has other opportunities that are not specific to CFS patients and their families, but could be helpful:

- Medicaid eligibility will expand greatly in 2014. Right now, eligibility is determined state-by-state, and in many states, Medicaid is really for mothers and children. Under the ACA, income requirements will now be the same in every state. This means that Medicaid eligibility will also be the same in every state. Many more low-income, uninsured people are going to be eligible. That is going to be an opportunity for people with CFS who are having trouble getting insurance.

Ms. Perry: The one thing that I would correct is that right now, Medicaid is also available in every state to the elderly and to people who have been determined to have a disability, but in certain categories. ACA has created a new coverage category where eligibility is based only on income. A person does not have to have any other specific characteristics to be eligible under this category.

- The current pre-existing condition insurance program, which is a bridge program, will be discontinued after 2014 and to be replaced by permanent regulations against turning people down for insurance based on a pre-existing condition. In the meantime, the bridge program is an opportunity for people to pay for health insurance at reasonable costs and avoid being denied because they have a pre-existing condition.

- Under the ACA, people who must buy their own individual plans and who have an income of 400% of the poverty level or less will get assistance with paying their premiums. This will take effect in 2014.

Committee Discussion

Dr. Levine: What are some of the down sides of the ACA? Is it that providers are going to be paid 30% less for Medicare as of January 2013? How will this affect deniability of claims? In other words, let's say a CFS patient goes for a tilt table test or other procedure. One of the offsets of providing affordable care to everyone will be that the providers get paid less.

Ms. Perry: I don't believe that's correct.

Dr. Lee: We can check into that. You know, Susan, there's a lot of misinformation that goes out about this Act because it has political implications. I'm not saying that what you're saying is wrong.

Dr. Levine: It depends on which administration comes into office too, I think. It was in the *New York Times* that the way the government is able to pay for the ACA—the money has got to come from somewhere. If providers are going to get paid less, will appeals of the denial process be affected?

Ms. Perry: I'm wondering if what you might be referring to something that people call the "doc fix." That is not related to the ACA at all. There was legislation passed a number of years ago that changed reimbursement to physicians under Medicare. The formula worked out in such a way that payments are lower than what people are comfortable with. Every year since, Congress has acted on a year-by-year basis. Reimbursements get set for that year, and that year only. Congress hasn't made a permanent change.

Dr. Levine: Depending on which administration we get, that might affect payments to physicians and other providers.

Dr. Lee: We can certainly look into that. Elaine, this is part of both of our day jobs, I think. The doc fix gets media play every year.

Ms. Perry: What has tended to happen is that near the end of the year, reimbursements get fixed for one more year.

Dr. Levine: What mechanism does NIH use to reach out to other doctors who may not have identified themselves as being interested in CFS but who you think might be? This includes practicing physicians as well as rheumatologists and other specialists.

Dr. Maier: The great part of the working group is that there's representation from many of the institutes and centers. Those are experts in their areas, such as the Institute on Allergy and Infectious Diseases or the Institute on Neurological Disorders and Stroke. There are many people who are program officers and individuals who have expertise in a certain area. As a group, we decide to reach out to people through going to conferences and meetings. Any time a WG member is at a meeting and is talking to potential grantees or talking to researchers, the WG member will encourage them to apply for funding opportunities. If we see someone who has a specific technique, methodology, or approach that might be unique and that might facilitate research, we will reach out to them. We have not yet reached out to physicians through physician groups.

Dr. Cook: When investigators are preparing their grants, they will often contact a program officer to help with development of the question being asked and with making it more appealing to a particular institute. Because CFS doesn't have a true institute home, would the WG be able to offer that sort of assistance to investigators, or should they still be going to program officers?

Dr. Maier: Investigators can contact program officers at any institute or center for any information or for technical assistance in applying for a grant. You're right; there is no institute for ME/CFS. However, ME/CFS is a very complex illness and the complexity of the illness really lends itself to a trans-NIH perspective. If an investigator has questions or is trying to find the best place to submit an application, he or she may already be coming from a specific approach. An investigator who is looking at aspects of care and caregiving might go to nursing. If there is a neurological aspect, that investigator might go to neurological disorders and stroke.

Remember, the applications that are received that have ME/CFS in the title or anywhere in the content or research plan will be going to a specific review panel. If the application scores well and is ready to be funded, it will be picked up by a specific institute or center at that point for funding. The Office of Research on Women's Health does not have delegated funding authority, but we have the ability to co-fund. When applications come in that are focused on women's health—and ME/CFS is a disease that affects women more than men—we can co-fund those applications.

Dr. Cook: Wouldn't your group be the ideal group to help develop an idea or question before sending the grant out for review?

Dr. Maier: The program announcements that are currently out were developed by the WG, so they capture the essence of the WG's ideas about what would be the priority areas for research in ME/CFS. That was part of the WG's task—to write those and send them out. You're right, it's complex because we have to be able to bring in the applications and assign them to an institute or center for funding. I am always available to do technical assistance consulting for anyone who's interested in submitting an application regardless of what area it's in. If I don't know anything about disease XYZ, I will find out.

Dr. Cook: This is the circular problem that CFS investigators have. There's no home to go to. We don't have that program officer to help us tweak the application in a certain way so that it is more attractive. Those grants that go in from ME/CFS investigators are already at a disadvantage because they didn't have that one-on-one assistance from a program officer. It seems to me that the WG is the perfect avenue for this. If we could develop that mechanism within the WG, we would give ME/CFS investigators the same advantage that all the other investigators for other illnesses have.

Dr. Maier: I hear what you're saying. I would still point out that the individuals who wrote the program announcements and who were involved in developing those are the same program officers who are listed as potential contacts.

Dr. Cook: Thank you for the explanation. My second question is, I'm curious as to the details of the collaborations you're seeking, such as the NIH Pain Consortium. It seems like an excellent collaborative opportunity due to the overlap between pain and fatigue. The consortium has developed its presence over time, become larger, and is instrumental in the Road Map Initiative. Can you give us more details of the collaborations that you're seeking?

Dr. Maier: What we are trying to do when we seek out a collaboration is to leverage resources and expertise. We are interested in working with the Pain Consortium because many of the representatives also serve on the Trans-NIH CFS Working Group. There is significant overlap in the interest and involvement of the individuals. As you said, the consortium is further developed and has a lot of financial support from stakeholders and Congress. There is a significant amount of interest in what the Pain Consortium is doing and how it is moving forward. We would like to be part of that to move our own agenda forward. We admit that we are still young. I'm new and I'm still learning. The WG has in mind to combine and collaborate with whomever is available to move things forward.

Mr. Krafchick: One of the important things in the ACA is the appeals process for denied claims. With health insurance claims there's a particular problem because if you have to hire an attorney, how do you pay the attorney? There is not typically a fund that is available. It might be worth considering some provision for attorney fees.

Ms. Holderman: You mentioned that HRSA was distributing the CME. Is it the CME collaboration with Medscape or the current CME on the website?

Dr. Willis-Fillinger: It's the CME developed with the support of the CDC that is on Medscape.

Ms. Holderman: You mentioned that you provide materials to educate about CFS. Which materials are you providing?

Dr. Willis-Fillinger: I said that the CME was distributed with an explanation of why it is important for our grantees to take a look at it. I can tell you what the explanation says: "Chronic fatigue syndrome is a complex disorder characterized by overwhelming fatigue that is not improved by bed rest and that may be worsened by physical and mental activity. Because the cause or causes of CFS have not been identified and no specific diagnostic tests are available, diagnosis and management of CFS can be challenging to healthcare providers. The Secretary has asked agency leadership to commit to an action plan and develop a department-wide strategy to address chronic fatigue syndrome. HRSA has been involved in this work and has agreed to disseminate information about CFS through our various communication channels. Our sister agency CDC has launched a CME that is entitled…," etc. We direct them to Medscape and ask for their feedback. Over the next few months I'll be following how the distribution went, who got it, etc. I'll give an update at the next CFSAC meeting.

Ms. Holderman: I wish that it would have included a bit more verbiage about CFS because, like the CDC website, it stops short with fatigue and doesn't go into anything more.

Dr. Willis-Fillinger: This is an invitation to clinicians to take a look at the CME. Clinicians love CME. It's required for us to keep our licenses. Just the fact that CME is attached to it means that people will spend that lunch hour reviewing it and getting the CME credits. I understand what you're saying. At HRSA what we wanted to do is get it in the hands of clinicians who are actually serving those millions of patients and make sure that they take the course.

Dr. Fletcher: My laboratory has been funded quite a bit by NIH with the specific aim of developing biomarkers in ways to not only diagnose CFS but to follow patients under treatment by clinicians. This work has been published in peer review journals. Everything that goes out about CFS says there's no test that you can do. We are moving towards the level of Great Britain where physicians can't order anything on patients who have CFS except behavioral modification and exercise. I don't know when this is ever going to change. I'm all for the primer that was put forward yesterday, but it's just like every other thing that goes out saying that there are no tests that you can do. At what point can we move beyond that?

Ms. Perry: I think that's a really important question. I don't know how qualified I am to address it, but I'll say a little bit. Publication in peer review journals is often a criterion for saying whether or not something is in the experimental or investigation status. One approach if claims are denied is for people to appeal and take the research to the insurance company to contest the denial. Having more evidence and more research is the ideal.

Dr. Fletcher: I presented at the NIH-sponsored workshop about immunologic markers and that didn't seem to make any major impact. The problem is the insurance companies. If a physician puts CFS down on a requisition for a test, that's a death knell for it ever being paid for. The physician has to think of some other diagnostic code to put on the requisition for the test.

Dr. Levine: If somebody sends out, say, a natural killer cell function test to your lab and the patient is a Medicare recipient, is that test covered?

Dr. Fletcher: Sometimes, but it revolves around what diagnostic code is used.

Ms. Perry: I can go back to our agency and talk to our coverage people and get more detail about what the Medicare coverage looks like for these kinds of tests for CFS.

Dr. Fletcher: I know there's a big push to limit the number of unnecessary tests with the meritorious aim of reducing healthcare costs. But we're not talking about things like doing prostate tests for specific antigens on every man over the age of 50, which—particularly for those over the age of 80—is silly. They will be positive, probably, and could result in harm to people.

Ms. Perry: Maybe you could give me the specifics about some of the tests that typically would be ordered and are typically not covered and I can look into our policies on that as a start.

Dr. Cook: Just to be clear, I think part of the problem is that with the evidence for biomarkers, we're still at the "associated with CFS" stage. We're not at the causative stage yet. Until we get to "If you manipulate this biomarker, CFS gets better" or "this biomarker is so unique to CFS that it has to be the causative mechanism for the illness," that's what is going to be necessary. These biomarkers are associated with CFS. There has not been any data to show they are causative.

Dr. Fletcher: I think that's a misinterpretation of what a biomarker is. HIV is a definitive biomarker. But there are many other biomarkers that are used to help the clinician follow the patient and understand how the person is responding to treatment. These are also biomarkers and they are very important.

Dr. Cook: It's not a misinterpretation; it's *one* interpretation of what a biomarker is.

Ms. Holderman: I agree, and I remember Nancy Klimas saying for so long—she went on record saying we have biomarkers. I think what we are talking about is subsets. Until we define subsets, people will continue to be able to deny that there are biomarkers for CFS when there really are biomarkers.

Dr. Levine: There are not only biomarkers, but tilt table tests, among other tests, that we use to fine-tune our treatment.

Ms. Holderman: For certain subgroups.

Dr. Lee: That's a biomarker too, if you ask me.

Dr. Dimitrakoff: Just listening to Mary Ann and Dane, I think everyone has a valid point. There are different types of biomarkers. There is a disease-specific biomarker that you can only find in a specific disease and that you don't find in any other diseases. Then there is a therapeutic biomarker that goes up with disease activity. If the disease gets worse, the biomarker will go up and if you give a treatment, the biomarker will go down. Cholesterol is one of those specific examples. I think that we probably have different subsets of biomarkers. I am not aware of a disease-specific biomarker in CFS so far. I think that the bigger question is, how to we get a research biomarker to become a clinically accepted biomarker? I think there should be a process where you can take a biomarker from the bench to the clinic and use that biomarker as a common tool.

Dr. Cook: To Mary Ann, the primer is an evolving document and they would welcome input from your laboratory saying these are the biomarkers we believe are useful in the clinic that should be included in the list of tests to send out on samples.

Dr. Lee: We are into our next hour and this is a question that we might want to bring up this afternoon. Would that be OK?

Funding and Other Support

Dr. Lee: The idea for the funding session came out of the Ad Hoc Workgroup. While there isn't much targeted funding for CFS, there are actually many opportunities for funding that we should all understand. I really appreciate Susan's discussion, for example, because NIH is the big gorilla when we talk about research funding. It has much more than any of the other HHS agencies combined. There are opportunities for the research community. Those opportunities have to be taken.

The vast majority of biomedical research in this country occurs in academic centers and research foundations. These are independent researchers. We at HHS cannot tell them what research they're going to do. We want CFSAC and the audience at large to understand the opportunities and to develop ways to nurture, to inform, to collaborate with academic researchers around the country, and to encourage them to apply for and develop these opportunities. The vast majority of research funds that are awarded by NIH are investigator-initiated. That means these are non-federal investigators who write a proposal, send it into NIH, and it competes with other proposals. That is a very important way that this business of funding research has been going on for decades.

I thought it would be a good opportunity today for us all to learn and think about ways we can encourage non-federal researchers to get into the business of applying successfully for these funds. We want to let them know that these opportunities exist. It's not just NIH funding.

AHRQ – Dr. Beth Collins Sharp

I appreciate being able to have this discussion because we heard over and over about how there isn't enough research and how frustrating that is. It's frustrating from this side of the money as well. I'm thinking of other discussions I've had with investigators or professional societies who come and say, "Come and talk about AHRQ and what the funding opportunities are." They always seem surprised that AHRQ potentially might be a fit. I'll tell you the messages that I give out:

1) **The project officer** – Call a project officer. I appreciate Dane's comments earlier because the most important message to highlight is to call a project officer and to have, if you don't already, a two-page concept paper. The first question that a project officer is going to have is whether there's a fit with the particular agency or within a particular RFA.

   When people call me, they often are thinking about one particular request for proposal and I might actually point them in another direction. This is an important point because I may in fact refer somebody somewhere else. I or any project officer may say, "Sorry, it's not a fit. Why don't you try somewhere else?" That's a hard message to deliver, but I think it's important so that investigators don't waste time applying for grants for which there's not a good fit. A proposal takes a lot of work to put together. It may take several rounds before a proposal is actually funded. We want to make sure it's a good fit and if not, refer you somewhere else.

2) **The team** – Once we determine that it's a good fit, we look at the team. Is the research team going to be able to do this research? Sometimes creating a good team means that you need to bring in collaborators who may not even be in CFS. Your strategy may be to become the second investigator, for example. After 20 years in an academic setting, I know what the pressures are to be the principal investigator and get the funding.

   In the long haul, it may be that you sign onto somebody else's grant. Who, for example, would not have loved to have been in the room when Project Echo or other similar projects were being developed and they said, "What disease are we going to focus this telemedicine project on?" Don't you wish you had been there and said, "What about CFS? That would be a good model for this particular intervention." You may make connections with other investigators who you might not think of otherwise. Susan gave the example where the researcher from the nursing institute has been introduced to CFS and now will be taking a closer look.

   One way you can make friends with investigators who you might not have thought of before is to look at other research that has been funded by a particular agency. This is important for several reasons. It tells you if there is a fit, it gives you an idea for potential collaborators or consultants, and if you find out it's already been done, you'll know it's going to be a hard sell for additional funding. We want to spread the money out as much as we can.

3) **The concept** - Because AHRQ portfolios are a little bit different and the funding stream may be different, you may need to think about adjusting your concept to fit. That's not adjusting your research necessarily—nobody would recommend that. But there may be a wrinkle to it that you had not thought of before or the focus of a particular area may be evolving.

   For example, our patient-centered outcomes research or comparative effectiveness research portfolio started out being funded by the Medicare Modernization Act and the focus was on the

health services for Medicare and Medicaid populations. Then the Recovery Act came along and comparative effectiveness was one of the provisions in that funding stream. Now there are ACA provisions that are funding patient-centered outcome research. With each of these there has been a little wrinkle as the science evolves and the topics evolve.

The other thing to say about the ACA funding is that it is a stream of money for which the tap is now just being opened. Assuming positives moving forward, this stream will continue. That tap is going to a number of places and AHRQ is one of them. I can't think of a place where research needs to be more patient-centered than in ME/CFS. Here's an opportunity with patient-centered outcomes research (PCOR) and this funding may be applicable to you. If you were to call me up with a concept, we could talk about how that might apply. But I may say to you that you need to go talk to NIH because the ACA funding stream is also going to NIH and the Private Public Partnership Institute. These might be a better fit for you.

So for example, with the PCOR dollars, we at AHRQ are focusing on methodology, dissemination, and training. That's a real specific focus. There may be something in that that fits but that's a little bit different than what NIH and the Private Public Partnership Institute will be focusing on.

4) **Registry of Registries** – I wanted to give you an example of one of the methodology projects that is being worked on right now. Information about the Registry of Registries was just published in a white paper on May 31st. By way of background, agencies have done a fair amount of methodological work on patient registries. There is a registries handbook, which is a wonderful resource. You can find a lot of technical support. It's in the second edition and the third edition is coming now. Some of the drafts will be out for public comment. I recommend those of you who are interested in patient registries to take a look at that.

   At the same time, AHRQ recognized that there was a need for what we're calling a registry of registries. It is along the model of Clinicaltrials.gov. There is one central searchable database to find out about patient registries. The power of these registries is amplified by having similar data elements and creating the operational methods so that everyone can benefit. There can be a transparent sort of process.

Dr. Lee: I have a couple of addendums to my earlier remarks. First, most of the money that goes out of the federal government for biomedical issues is research, but there is some that is not research. The second thing concerns the last meeting we had during which there was a talk about the need for NIH specifically to reach out to CFS researchers and court them. I think that's a difficult task for all of these agencies to do. CFS is not the only agenda item for research or other activities. We have these existing mechanisms for funding for many, many biomedical issues.

But I think there's real opportunity for the energy that I see over and over again from the patient groups to collaborate to nurture academic researchers and help them come up with ideas. It happens all the time with many advocacy groups. I think there's a real opportunity for the patient organizations that have CFS as their mission to really work with academic researchers to build the capacity and the funding that they could get for CFS through these existing mechanisms.

CDC – Dr. Ermias Belay

CDC does not have investigator-initiated funding opportunities for CFS or other diseases in the same way that NIH does. It's just not our mandate. Having said that, we have specific budgets for CFS that range between $4 million and $5 million a year. A good chunk of that funding is used to pay for the kind of activities that I described yesterday:

- Provider education, such as the CME credits and the standardized patient. We have a contract with an outside agency to develop that standardized patient for medical school curriculums. Provider education is also paid for through a contract mechanism.

- The seven clinic studies. We use a cooperative agreement mechanism, which is different from grants, investigator-initiated R01s, and the other funding approaches that NIH uses. Cooperative agreements are competitive and open to researchers, but the research and projects are initiated by the CDC.

- The pathogen discovery with the institute in California. That's a specific contract. We have a specific scientific question that we want to address and then we target funding to a specific laboratory. I will check on whether it was competitive. I think it is a contract. If it is a contract, it doesn't have to be competitive.

Dr. Lee: I'm emphasizing the competitive part because that could be an opportunity for people to come in with their applications.

Dr. Belay: When we put out a cooperative agreement, it's for anyone to submit applications.

Dr. Lee: Our plan is—and I think we've done this in the past—when specific CFS opportunities come out, we can then put a notice out on our website with a link and publicize the opportunity through the listserv.

Dr. Belay: It is usually announced on Grants.gov, a government-wide website.

[**Dr. Lee** paused the presentations to welcome Dr. Lisa Corbin who arrived after a delayed red-eye flight.]

Dr. Lee: We really appreciate your effort to get here. Dr. Corbin is associate professor in the Department of General Internal Medicine at the University of Colorado, Denver School of Medicine. She serves as the medical director of the Center for Integrative Medicine at the University of Colorado Hospital. Dr. Corbin was instrumental in establishing this clinic, sees a diverse set of referred patients for CFS and FM, and uses complementary and alternative medicine approaches to care for patients. She is an expert in complementary and alternative medicine and incorporates these principles with traditional medicine in her practice. She also conducts research in chronic fatigue and pain through the incorporation of integrative medicine.

CMS – Alaine Perry

The list of websites that I handed out contains the link for the Innovation Center, which I'm going to talk about. As I mentioned in my earlier presentation, the CMS Innovation Center was one of the products of the ACA and was established to test innovative payment and service delivery models to reduce program expenditures in Medicare and Medicaid programs, while preserving or enhancing quality of care for patients. The goal is to make transformations in the healthcare system where improvements and innovations in the healthcare system, quality of care, and access to care for patients can be made at the same time that costs are lowered.

The center's basic process is working with a very broad range of stakeholders to solicit ideas for innovative models, then selecting and developing those models to test and evaluate them. The center then works to disseminate more widely the models that are successful. The focus is on Medicare, Medicaid, and the Children's Insurance Program—the programs that CMS runs—but the center is interested in

things that can also be applied more broadly. It's really about seeking better ways to do healthcare, not just the Medicare and Medicaid programs.

Some of the kinds of models that the center has been developing or testing include:

- Telemedicine
- Integrated multidisciplinary approaches to care
- Using non-physician care to extend capacity
- Care coordination
- Increasing emphasis on primary care
- Payment models such as providing compensation for care management

A lot of the programs are general and would apply across different diseases, but there are also some disease-specific programs. The center does grants for programs on chronic pain, stroke, and asthma, just to give a few examples. The same organization that did Project Echo is now getting some funding from the Innovation Center.

Healthcare Innovation Grants

These were announced in the fall. The applications for the first round were closed in the winter and some grants have actually been awarded. A decision has not been made on whether there will be a second round. I will keep CFSAC informed about the situation.

Innovation Center Pipeline Process

- This is a unique approach. The center is inviting any stakeholders to come up with models for the center to test. People within or outside of CFSAC or any other group could collaborate on a model.

- I would be happy to provide technical assistance and brainstorm ideas. The Innovation Center is very open to providing technical assistance.

- What the center is charged with is finding innovative ways to lower healthcare costs and improve quality at the same time. Lowering costs could be in the short- or long-term. One thing that the process does require is development of a clear business plan and a convincing demonstration that the proposed would put CMS on the path to both improving quality and reducing costs. The business plan must have numbers, figures, and a strong rationale for how it would work.

- The center encourages collaboration with other HHS agencies.

- The door is completely open to brainstorming about a lot of the things that we've been talking about, including something similar to the Project Echo model. We would have to have brainstorming conversations about what type of model would be helpful to people with CFS and advance healthcare for this population while also meeting cost-saving criteria.

- What's interesting about the process is that after the center accepts a model, it would go out with a solicitation that could be done through a cooperative agreement, grants, or contracts. At this point, it would become a competitive process. It would be open to anyone who meets the criteria and wants to submit an application to test the model. The group who came up with the model could compete, but it wouldn't necessarily be selected.

Food and Drug Administration – Dr. Theresa Michele

- FDA is a fundamentally different agency than many of the others you have heard from because we are a regulatory agency. We are responsible for regulating a large portion of the consumer products that people use every day. This includes some things that don't necessarily apply to CFSAC, such as the foods, veterinary products, and tobacco products.

- The three groups at the agency that focus more specifically on health products would be:

    - Center for Biologics Evaluation and Research, which does vaccines and blood products.
    - Center for Radiologic and Devices. The name explains its areas of interest.
    - Center for Drug Evaluation and Research. This is the one I'm going to focus on because it's the area that applies most closely to the work of this committee.

- Just to correct one misconception I heard in some of the advocacy groups—there was a request put out yesterday to accelerate the FDA pipeline for ME/CFS. We don't have a pipeline. We don't have a pipeline for asthma or cancer or anything else, because we don't conduct drug development. What we do is regulate drugs that are in the process of being developed and that are out in the market. The pharmaceutical companies have a pipeline. We try to facilitate that process by making sure that the products that get out on the market are both safe and effective.

- We don't really fund drug development either. That's up to the pharmaceutical companies, individual investigators, or whoever else is out there doing drug development.

- There are some opportunities, though, for facilitating this kind of development. Sponsors actually pay user fees whenever a product comes to FDA for approval for marketing. There are several situations under which those user fees are waived:

    - **The first approval of a drug by a small business.** That is written right into law. There are specific criteria of what qualifies as a small business. If a company qualifies as small and does not have a product on the market yet, the business can qualify for a waiver of the user fee. With that said, these companies put a lot of money into drug development before they get to the user fee stage. The business has done all the testing and is ready to put the product on the market.

    - **Orphan products**. To qualify for orphan status, a drug has to treat a disease suffered by fewer than 200,000 individuals in the United States. There are many people now with CFS. The actual numbers vary depending on whom you talk to. Once upon a time years ago, CFS did qualify for orphan status, but it no longer does. If a new company comes to us and asks for orphan drug status, CFS does not qualify at this point in time.

    - **Pediatrics.** Companies do not get waivers of user fees for drugs serving a pediatric population, but they get additional marketing exclusivity, which ties into a great deal of money. Once a product is on the market, a company can ask for a pediatric-written request. If the product qualifies through being supported by correct pediatric studies, the company can get an additional six months of marketing exclusivity.

I also refer you to our website. There are links there to the Small Business Administration (SBA) where grants and loans are available that could be used for drug development.

Go to www.fda.gov

Click under *CDER*.
Click under *Industry*.

There are links that will take you out of the FDA website to SBA. There are specific grant mechanisms there that can help with drug and product development for small companies.

Dr. Lee: Just to reemphasize the point, this is another opportunity for our research, advocate, and patient communities to partner; this time with drugs and drug developers. We even had one of the drug companies speak yesterday during our public testimony, so you know who that person is. Maybe you can partner with him. These are opportunities to put the energy I see in the committed people around CFS into finding new partners, new collaboration, and nurturing opportunities.

HRSA – Dr. Deborah Willis-Fillinger

As I said, there isn't much from HRSA because we are an organization that supports direct care services, community organizations, and other not-for-profits that provide direct care or infrastructure support for healthcare services. We don't have specific funding for ME/CFS or other specific diseases.

I gave the example back in November of the Family-to-Family Network that was being funded. Those awards were announced in May. There isn't anything similar at this point. We do have a website—www.hrsa.gov—with a link for funding opportunities. Between now and the next meeting, it would be useful to keep an eye on that site.

Dr. Lee: If you'll let us know, we can add it to the CFSAC website and send out the information on the listserv.

HHS – Dr. Susan Maier

In my presentation earlier I highlighted what really is the thrust of NIH in terms of supporting research. That was the use of investigator-initiated versus targeted research—solicitations if you will—to stimulate or encourage a field of research in a specific area. We actively seek out potential investigators when we go to meetings in our specialized areas of expertise. Whenever an individual goes to a meeting, he or she is always a target for researchers to speak with. That is part of our job—encouraging people to apply for research in any and all areas in which they are qualified and eligible.

Potential Opportunities for Collaboration

There are limited funds and there are a lot more people seeking funding. When I was younger and seeking funding, it was one investigator, one grant. If you were lucky, you could get two grants funded. That world is going away very rapidly. We are in a team environment. We are in a multidisciplinary research environment. We're in an environment where the techniques that are available are expensive. Technologies are not cheap. If you want to look at or do MRIs, genomic testing, or any other advanced testing, those resources are expensive. It's no longer a period where researchers can just apply for a grant, get that grant, and do all the research that this world now demands.

NIH is trying to leverage the money we have as much as we can to bring people and resources together so that the infrastructure support is available.

What I think would be a great idea and something that everyone can advocate for is the development of repositories—repositories for biological samples and data collection of any type. This presents an opportunity for secondary data analysis once you have a repository of already-collected data and samples that are harmonized. If my research question is different from the next person's research question, but we

still need the same type of data, we can ask those different questions. Even if we don't find an answer or our answer is unclear, it's a source of information that would present an opportunity for hypothesis testing and for hypothesis generation. We're not limited by collecting data. I have a set of data; now what can I ask? What kind of hypothesis do I have and can these data help me? Secondary analysis is a very inexpensive type of experiment.

Dr. Lee: Will NIH fund applications for such patient data registries?

Dr. Maier: An opportunity always exists for individuals who would like to submit an application for developing a repository, yes.

Even when there is a targeted solicitation or funding opportunity announcement out there—on ME/CFS for example, we have to receive applications in order to review them and potentially fund them. There are not many applications submitted for ME/CFS. This is a problem, because if we can't get the applications in, review them, and fund them, then they can't fund ME/CFS research.

I know the thing that is popping into everyone's head is, "Well, hello, why don't you just issue an RFA? Put some money behind it. Put some teeth in there." Even if we put out an RFA and attach funds to it, there is no obligation to spend that money if the applications are not well-crafted and they do not address the questions that are asked or suggested as areas of research within that RFA. Even if applications do come in response to an RFA, there's no guarantee that research will move forward if the applications do not score well or do not address the questions that NIH is seeking to answer.

This is something the WG is struggling with: how do we get people to submit applications? How do we get them in? That's why we're trying to do outreach by attending meetings and reaching out to people in the ME/CFS field as well as to those who are not in the ME/CFS area but have unique approaches and ideas. We want to let those people cross-communicate. Let the research suggestions and ideas cross-fertilize to move the field forward.

Dr. Lee: Susan provided a PowerPoint with lots of details that will be available on our website as soon as we get it in compliance. I've heard this before in talking with Susan and with other leaders from NIH. If they don't have a lot of applications through the RO1 process, there's concern that there is not a research community out there that can respond to a more targeted RFA. Again, here is an opportunity for the CFS community—researchers, patients, and advocates—to really build, nurture, collaborate, and work with the academic environment to build those.

Committee Discussion

Ms. Holderman: When you say RFP, is that synonymous with RFA?

Dr. Maier: Yes. Technically, an RFA is the terminology used for grants and cooperative agreements in the NIH world. RFPs (requests for proposals) in the NIH world are used for contracts. Typically RFAs will have a set aside amount of funding dedicated at the time the solicitation goes out. Applications will come in and be reviewed. The applications will be awarded according to how well they scored until the money runs out in that set-aside. If there are insufficient applications within the set-aside, the money doesn't get used for that.

Ms. Holderman: I know that HRSA has a focus on AIDS, but everything else is not disease-specific. If that's the case—and I would never begrudge any disease group for getting anything—why AIDS and why not CFS when CFS has way more sufferers who tend to fall into the low-income population?

Dr. Willis-Fillinger: That's historical. The Ryan White Care Act was passed about 20 years ago. That was because at the time people were dropping dead, nobody understood why, and the numbers were increasing worldwide. There was a desire to provide decent services for that population. The reauthorization is being considered right now for future years and future funding. Now that there is treatment available to HIV/AIDS patients for both care and prevention, those funds may be diverted into basic primary care in the future, but at present, I can't explain it any other way.

I think the size of the epidemic, the political support and advocacy around that particular disorder, the catastrophic impact of HIV/AIDS in terms of its infective nature and spread—there are lots of other reasons why that particular disease is a high-profile disorder and particular care was needed. Part of the challenge is not only that there is a catastrophic impact that continues to spread but also that there is a fair amount of education that needs to be provided to the public about prevention and appropriate treatment in order to stem that epidemic and control it.

Dr. Levine: Beth, could you explain to us what a registry entails? And then I wanted to ask Alaine, please, to give an example if she could of the kind of coordinated care that CMS is looking for. What would be an example of applications? What would be an example of the cost reduction you're looking for?

Dr. Collins Sharp: A patient registry is a centralized place where data about individuals is collected in order to follow them through time and evaluate a number of treatment options, natural history…

Dr. Levine: Could you search under a subheading of sorts, like hepatitis C for instance?

Dr. Collins Sharp: In terms of the registry of registries?

Dr. Levine: How would you search for a disease that you're interested in?

Dr. Collins Sharp: You can search by disease, by age range, and by a certain treatment to see where treatments are being used across registries. While we are talking about registries, the strongest from a health services perspective are those that include biologic and clinical data—more patient-centric data. It may not be just clinician-reported data but also patient-reported data, as well as biologic data. Bringing it all together creates the strongest database. It makes a significant difference when you include the clinical data with the biologic data and then the next generation, which includes patient-level data—quality of life and patient-reported symptoms.

Ms. Perry: I'm not going to be able to give you a model in any significant detail. You can get a lot of details from the Innovation Center website about what they've currently funded and different models that they're testing. An example of care coordination would be paying a primary care organization an additional care management fee to help track the care of a person with multiple conditions. This may include tracking the specialists the person is seeing or using telemedicine to check whether he or she is adhering to the different regimes.

Although more healthcare procedures may be reimbursed, there would be savings down the road because the person would stay healthier, better care would reduce hospitalizations, etc.

Break

Public Comment

A summary of public testimony appears at the end of this document.

Lunch Break

ME/CFS Organizations

Dr. Lee: Before beginning the session, Dr. Lee commented on two areas. The first was questions that have been raised about the inability of foreign scientists and other foreign visitors to attend CFSAC meetings. She noted that a scientist from Norway attended the November 2011 CFSAC meeting, which was held at the Holiday Inn. She explained that hotels do not have the same security requirements in place to screen those without a U.S. passport. Thirty days notice is required to clear a person without a U.S. passport to enter a federal building. CFSAC staff does not routinely reject foreign guests, but staff needs at least a month's notice to clear the person for entry into the building.

In her second comment, Dr. Lee said that, "I just want everyone to know that all of the people up here, both our non-federal committee members and our federal committee members, are committed to this topic [ME/CFS]. We have worked hard. Some people have worked for many years and we are very committed to this topic and that's why we are here. We have several of our government members who are personally affected by CFS. We are very committed to this or we wouldn't be here.

CFIDS Association of America
Kimberly McCleary, President and CEO

- CFIDS Association is marking its 25th year of service. I'm going to limit my remarks to what we are doing currently because I think that is more relevant.

Transformative Research

- Over the last four years, with the addition of a full-time scientific director, Dr. Suzanne Vernon, we have narrowed our focus to stimulate research and build, nurture, and collaborate with the scientific community so that there is more robust CFS research, both in terms of the number of topics being studied and the rigor.

- We launched the Research Institute Without Walls on February 23, 2012. We are now focused on identifying disease-modifying treatment for CFS. We narrowed in on that as an area where nobody else is looking very closely right now. Hopefully our research is feeding into building a pipeline where we'll work more closely with the FDA to put products in for evaluation.

- There has been confusion over our role in patient advocacy. What we are doing is expressing our advocacy through our research program. The advocacy community sort of struggles with the labels, of which one of us is patient advocates. I think all of us in the room are patient advocates or we wouldn't be here, as Nancy said.

- In 2009-2010, we had six grantees that were able to turn $637,000 in seed funding into follow-on grants from NIH and the Department of Defense totaling $5 million. That's the model that we've been hearing about this morning—researchers with pilot data and early studies who go on to compete successfully at NIH and other agencies for investigator-initiated awards.

- In March 2010 we launched the SolveCFS Biobank with assistance of infrastructure provided by Genetic Alliance. To date we have enrolled 482 participants that include individuals with well-characterized CFS—many of them coming through clinicians who have either served on this committee or presented to this committee—as well as contact controls and healthy controls. Since March 2010, we have launched nine research projects. For the sake of comparison, in that same period of time, NIH has launched seven CFS-specific research projects.

- Last year, in order for us to refine our scientific approach, we formed a diverse Scientific Advisory Board that includes people who are or have served on CFSAC and researchers from top institutions in the United States and Canada. The samples and clinical information from researcher shown on the left of the [SolveCFS Biobank] slide Dane Cook, post-exertional brain and blood markers; Peter Rowe, neuromuscular strain biomarker; Marvin Medow, intervening in orthostasis-induced dysfunction will feed into the SolveCFS Biobank to be used by researchers on the right of the slide. Many studies are focused on finding biomarkers or consistent objective evidence that we would push further down the pipeline for diagnostics and treatments.

- Dr. Maier brought up drug repurposing in her talk. CFIDS is working with a small company called Biovista to look at some of the drugs that have already been approved for other indications and what utility they might have in CFS. These are non-obvious drugs. We're not just looking at the medicines that are typically in the arsenal for symptom relief. We're looking more deeply at some of the mechanisms of action and how they might work in CFS.

- I was at an NIH meeting on Tuesday and heard the National Human Genome Research Institute Director talk about the value of epigenetics and complex diseases. We are delighted to have a young investigator, Patrick McGowan, looking at epigenetics in CFS for the first time.

Vibrant Communications

- We are pairing research efforts with communications. We know how important it is for people whose lives are impacted daily by this illness to know what is going on. Our communications efforts include:
    - A semi-annual print publication called *SolveCFS*
    - A research-focused website launched last year called Research1st.com. The site has 212 posts on research topics, many of them written by guest experts.
    - "Research1st News," a monthly e-newsletter digest of research and policy news.
    - A series of webinar programs (25 so far). A webinar is scheduled for the end of July on post-exertional malaise and relapse.
    - An active social media presence on Facebook, Twitter, and YouTube.

- We've learned how to structure a research program from organizations such as the Michael J. Fox Foundation and the Susan B. Love Army of Women. Now we need to take those models and figure out how these organizations raise money to support illnesses so that we can meet the needs and expand the research in a vibrant way.

Magnetic Growth

- I have pictured Bernie [Hillenbrand's] beautiful daughter Laura Hillenbrand because we are so grateful to her for the tremendous support she provided to help us get the Research Institute Without Walls launched this year. I'd like to be able to tell you the stories of the other catalysts pictured on the right. It's been a great coming together of people's interests really resonating throughout the community.

- We are beginning to host regional events that we call Catalyst Cafés to bring our message to individuals and use tools other than the impersonal internet in hopes of reaching more circles of people and getting them involved.

Speak Up About ME
Mary Dimmock on behalf of Denise Lopez-Majano

- Denise is the mother of two young men who became sick during their school years. Denise had to face problems with the school, being able to get the support that her sons needed, and social isolation. She became determined to find a way to help her sons, and out of that determination Speak Up About ME was borne. Its purpose is to help young people and their families better deal with the unique challenges that they face because of their age and what they must cope with in their lives.

- Denise wanted to be here but her two sons are too ill for her to attend CFSAC for more than a day. That's a challenge faced by many in this community—trying to advocate when they're too sick or too busy taking care of their families.

- Speak Up About ME assists young people and their families in three ways:

    - <u>By fostering the sharing of knowledge and information that addresses the unique challenges that these young patients face</u>. Examples of this kind of information are school accommodations to which ME/CFS students are entitled. We heard quite a bit about that from yesterday's panel. I won't go into it except to say that Denise has talked to me about examples where children are being asked to go into lower grade levels and lower level classes that do not challenge them from an intellectual perspective. The schools feel that these classes are all the children can handle.

      Another example is connecting parents with advocates—people with experience who can help families who are just beginning to deal with:
        - School issues
        - How the SSI and SDI (state disability insurance) processes work, especially with school-aged children and people who will never have a work history
        - Special needs trusts and other financial planning mechanisms. If you've never worked, you can only have about two or three thousand dollars in order to qualify for benefits.

    - <u>By providing approaches for dealing with social isolation</u>. It's very hard for patients to find someone who has been through similar circumstances. It can be very helpful when they meet somebody who has gone through exactly what they have experienced. Denise spoke about being able to connect two mothers who had two daughters, both with ME. One already had a toddler and the other was going through pregnancy. Those two mothers were able to talk to each other about that experience.

    - <u>By giving them confidence</u>. It's intimidating for parents or patients to face healthcare providers and school systems that tell them they are really not sick, they just need to get with it; they just need to try. They need the confidence to say, "No, I'm sick. I need this kind of support from you."

- Speak Up About ME is not located in a specific place. It's really a grassroots coalition or network of people who are focused on issues specifically affecting young people with ME/CFS. These include school issues, which doctors can help ME/CFS patients, pediatrics, and how to counteract the stigma of ME/CFS, especially when patients face schools and peers. A particular concern is how these patients make up for so much lost time during their formative years when they would have been developing life and social skills.

- The network is focused predominantly in the United States but obviously there are opportunities to share information with school systems and advocates in other parts of the world. Denise has established contact with some of those individuals to start to understand what they're doing and what is working within their population.

- Why do we do this? Because this is such an underserved population. You heard how underserved this population is and how unique their needs are in terms of getting services and support.

- The woman, Faith, on yesterday's panel spoke about regional groups that meet a couple of times a year. I have had the good fortune to be able to see how it really works. As she said, these patients can come together in a way that everybody understands what they are dealing with. They don't have to explain themselves when they have to lie down. It has a big impact on children and parents when they get to support each other and understand what is working. It's an excellent model to be replicated in other parts of the country to help school-aged children.

- Speak Up About ME maintains an ongoing list of patients who had early onset. Not all patients are still under the age of 23, but for anybody who has or did get ME/CFS under the age of 23, Denise maintains a list. Currently there are 120 people on that list.

- Denise wanted me to share with you a partnership between Speak Up and Phoenix Rising to develop a survey that looks at Social Security issues and Social Security disability for people with CFS. As of May 31, there were about 168 completed survey responses. We're trying to learn what factors ultimately result in successful SSI and SDI applications and how the length to final determination has changed over the years. The groups expect to have a report ready by the Fall of 2012.

Pandora
Marly Silverman, Founder

- I started Pandora basically out of self-necessity. I was trying to find solutions and better resources to take care of myself at the time I became ill with ME/CFS.

- Pandora has a unique niche. We embrace the concept of NeuroEndocrineImmune diseases (NEIDs), including ME/CFS, chronic Lyme disease, FM, multiple chemical sensitivity, environmental illnesses, and Gulf War illness.

- We approach these diseases from a quality-of-life issue because in most of the support groups that we supported over the years, patients had these co-morbidities overlapping constantly. People with ME/CFS would come in, and two years later be diagnosed with FM. People would come in with Gulf War Syndrome and have major FM and multiple chemical sensitivity issues. We realized that from a quality-of-life standpoint, it would be a much better approach if we embraced these under one umbrella.

- We have been very successful to the point that the New Jersey legislature passed a standing resolution pushing for an NEI Center.

- Our main advocacy program over the years has been the Advocates Extraordinaire Leadership Program. It started as a grassroots program and in 2007, we sponsored and hosted the IACFS/ME conference with grants from the community. It has been extremely successful. A lot of patients who testify before CFSAC are here supported by the Advocates Extraordinaire program.

- Pandora projects have included Empty Chair Project. Pediatric Pennies, I Need A Hero, and Quality of Life, a local project where we go to people's homes and help them with chores such as organizing their finances and decluttering their homes. Pandora created the Bringing Ryan Home project when a child was taken from his parents and his mother was accused of Munchausen's by Proxy. She was later charged with failure to provide primary care because she could not find a physician in her North Carolina County who knew how to treat ME/CFS. That family now owes $30,000 in lawyer fees and is still trying to find a primary care physician to treat their child. This is why we keep coming back to you to emphasize that quality-of- life issues are something that we struggle with every day.

- We also support the Coalition 4 ME/CFS, a group of eight organizations with a goal of jointly addressing the main hardcore issues that we are facing every day, including funding, research, the FDA, and stakeholders meetings. We are extremely successful because now other organizations are now joining us—not necessarily within the coalition—but joining the advocacy train. I am very grateful to Mary for helping me with the joint request letter to HHS that she read yesterday. It is a powerful letter because it was a united front from all of us.

- Over the years Pandora has provided grants to numerous individuals and organizations, including Drs. Nancy Klimas and Gordon Broderick, the Vermont CFIDS Association, the VA Foundation of South Florida, the National Fibromyalgia Association, and others. Pandora has also received grants, the latest of which is being the first to win a $20,000 grant from Chase Community Giving.

- It is important that the NCHS issue by addressed as soon as possible. ICD-10-CM has been postponed, but it has to be addressed.

- I do have one special thing that I want to address. Pandora would like SSI to consider the possibility of placing severe ME/CFS patients on the list of compassionate allowances. Because of the neurological findings of ME/CFS, we have a way to identify a severe patient who should be allowed under compassionate allowance. These patients would go through the process very quickly, the administrative law judge knows how to handle you in 3 to 6 months, and you have access to Medicaid or Medicare.

- July 1, 2012, will be Pandora's 10th anniversary.

Phoenix Rising
Cort Johnson

- I am president and founder of Phoenix Rising, which is now a nonprofit corporation.

- The phoenix is a powerful symbol of renewal as it rises from the ashes to new beginnings. It's that possibility of renewal that the patient community and staff and volunteers of Phoenix Rising are committed to producing.

- Phoenix Rising is different from other organizations. Working entirely online, we think of ourselves as the world's largest support group. As such, we are committed to providing information, tools, and opportunities that people with ME/CFS can use to make a difference in their lives. Currently we empower people by providing accurate information in a controversial field and tools to facilitate the free flow of information and break up the isolation present in this disorder. With more than 1,000 articles and pages on our website, more than 5,000 registered members, and more than 260,000 posts on our forums, Phoenix Rising presents an information resource second to none. At any given moment, between one and 200 people around the world are scanning Phoenix Rising's forums, website, chat rooms, blogs, articles, and newsletters for information on how to get well.

- We have changed dramatically over time. Begun in 2004 as one person's attempt to build an ME/CFS knowledge base, Phoenix Rising has become a diverse organization committed to using the power of the patient community to produce change.

- Recent patient-driven projects supported by Phoenix Rising include

    - Hosting the ME analysis of the PACE trial, which uncovered major errors in methodology and analysis.
    - Collaborating with the Coalition 4 ME/CFS to produce a critique and provide recommendations for the IDC-10 document.
    - Working with Speak Up About ME to product the first comprehensive disability survey in the ME/CFS community.
    - Most recently, supporting the effort to produce a stakeholders' meeting to advance treatment options at the FDA.

- Phoenix Rising's goal is nothing less than transforming the way chronic illnesses are supported on the web and in doing so to build strong communities capable of achieving change. Judy in Miami, for instance. Judy doesn't know anyone in her area to whom she can talk about ME/CFS. But what she doesn't know is that she is actually surrounded by patients and their supporters. Support groups and good doctors are available. She doesn't know this because that information is either missing or haphazardly presented on the web. By putting patients, doctors, volunteers, support groups, and research groups on the map, Phoenix Rising's "Community Rising" program will allow Judy to build vibrant new relationships, find support options that she didn't know were possible, help her find the best doctors in her area, and enroll in local research efforts.

- Meanwhile, Mary has seen six practitioners, Joan has seen 10, and both have spent more time and money than they could have imagined, simply trying to find someone who understands this illness. What if with one click they could see which practitioners in their area were the most effective or the best fit for their budget? Or which just happened to be really good at solving their dizziness or pain or sleep problems? Phoenix Rising's physician review program will not only determine which practitioners are the most effective, it will help identify which types of practitioners they are and how important experience is in treating this illness. Who gives patients the most bang for the buck? In short, the program will help patients decide who they should see to get the best results.

- The Phoenix Rising treatment review program will inform patients of the best treatment options and, as we produce and send out reports, inform medical doctors of options they aren't aware of.

- These are just some of the programs that Phoenix Rising will use to build a virtual community that empowers people with ME/CFS around the world.

New Jersey Chronic Fatigue Syndrome Association
Patty Strunck

Although our address is Florham Park, we're all over the state from just south of New York City to the very end by Atlantic City. Our membership and our board members are from all over the state. We are a 501(c) (3) nonprofit organization that was established in 1995. We

- Support patients and their families.

- Disseminate reliable information about the illness.

- Facilitate communication between healthcare providers and patients.

- Promote research into the cause, diagnosis, and treatment, and cure of ME/CFS.

- Educate patients, nurses, and others in contact with those with ME/CFS. One way we educate healthcare providers is by going to medical conferences.

- Sponsor support groups that meet throughout the state in various locations such as libraries and hospitals. Some support groups no longer meet because the leader is too ill to run the group. Some groups can only hold phone meetings.

- Run a helpline with a toll-free number that has taken 263 calls in 2012 as of May 31. Most calls are from people who want access to our physician referral list. That's easy; I can just shoot them an email with our list. Other times the person wants and needs a shoulder to cry on; somebody to listen. You can give them an hour more of your time. That's really one of the reasons why I do that job. It's rewarding when you're listening to somebody who was just diagnosed or doesn't know what to do because his or her family is not understanding and the person needs help. He or she doesn't know where to turn and you can give them some insight, information, and just listen, which is what the person needs at that point.

- Have a website is full of information.

- Provide a physician and an attorney referral list. The only way to access these is by calling our helpline.

- Publish a journal twice a year.

- Keep a lending library with more that 263 books and medical journals, the most extensive private collection of ME/CFS literature available. The library also has audio and video. All the material is available free to our members, but there is a mailing fee.

- Hold an annual medical conference in the fall. That year we had Dr. Beth Unger from the CDC come and speak. Dr. Lucinda Bateman will speak at this year's conference about ME/CFS treatments and signs and reasons for optimism. Natalia Palacios will speak about epidemiology in a large study of female nurses. Wilfred van Gorp will speak about evaluating the brain effects of CFS in children, adolescents, and adults. Dr. Susan Levine will speak about forming successful clinical research collaborations to conquer the enigma of CFS.

- Offer benefits to patients and their families:
    - A high school scholarship that is the only one of its kind in the United States that a group offers. The student has to be both educationally and financially qualified.
    - We were the first group of its kind to offer a medical school scholarship. The student has to attend one of the medical schools in New Jersey. We were the model for this medical school scholarship. Vermont CFIDS Association and Pandora are now offering one as well.
    - Medical accommodations help. Some of our board members sit in on Individualized Education Program (IEP) meetings to assist parents with accommodating their student.
    - We have CMEs for physicians and four information fact sheets. Coming soon is a new one, which is ME/CFS information for school nurses and school personnel.
- We had a consensus manual published in 2002 for physicians. We are hoping to update that manual with a pediatric manual.
- Every May, Gov. Christie declares May to be Chronic Fatigue System Awareness month.

Committee Discussion

Dr. Lee: I want to thank all five groups. They came here at their own expense and we greatly appreciate that. There are many reasons we thought this was a great idea. We hope to continue with this and in November, have additional panels of organizations committed to bettering the situation for CFS patients.

We are required to renew our charter every two years. I think it would be fabulous to add membership from these organizations. There are several other HHS advisory committees that have organizational members as non-voting liaison representatives. They wouldn't be able to vote, but they would be able to sit with us and speak when called upon. The CFSAC liaisons wouldn't have to sign up for the public comment. That time would be available to others. They would be able to participate in our discussions. I think this is a great idea. We are going to move forward with the charter process. It requires public comment and some careful thought. We have a requirement to get at least the initial draft done by this Fall. I don't think we'll be able to have huge numbers—we're talking three or four members. Our thoughts are that those organizations would have a term just like our membership has a term so that even though we are only able to have three or four the first time, we'll be able to replace those organizations over time with other ones. We haven't gotten further in the details, but I think there is a lot of commitment on our side to go forward. So, let me open up the discussion.

Dr. Casillas: I have a question for Cort and Patty. What criteria do you use in selecting the physicians who will be on your referral lists?

Ms. Strunck: In New Jersey we go by our own patient's recommendations. We have people who have referred physicians to us. Then we send a form to the physician to fill out and if he or she wants to be on our referral list, the person fills out the form and returns it to us. We don't do it without the physician's knowledge.

Dr. Casillas: Do you pick any specific specialties?

Ms. Strunck: We have lots of specialties on our list.

Mr. Johnson: We don't have a physician referral list. We are working on a physician review list where patients review the physicians. They will be able to weed out the better physicians from the not-as-good physicians. That's one of our goals—to try to get people the best physicians and stay away from those physician who aren't good or do harm.

Dr. Casillas: You'll rely on the patient description of their care for the basis of your decisions?

Mr. Johnson: Yes, we have a kind of a comprehensive survey, so we'll ask the patient to review the physician on all sorts of areas, and I think we'll be able to get some good data from that.

Ms. Silverman: In the case of Pandora, it's pretty much patient referral as well. We kind of follow the same process. We call the physician to see if he or she wants to be listed. We have had cases in the past where patients refer physicians to us and we had phone calls from the physician saying, "Please don't put us on your list because we can't accommodate the type of patient care it requires, time-wise and money-wise." It's not a perfect science, but we strive to get physicians who really want to take care of CFS or NEIDS patients.

Dr. Corbin: I have a comment and a question. What struck me, and I hope it struck others as well, is how much collaboration is going on among the five groups here today. I think that's spectacular because a lot of times it seems like when there is a cause, there are groups that wind up competing with each other for limited funding. The collaboration brings me a lot of hope.

My question is for the CFIDS Association. I'm intrigued by the biobank and a lot of discussion I heard today. How do patients get their bio into your bank?

Ms. McCleary: Our startup study was narrowly described. We were looking for a well-characterized patient with keen onset and must have the post-exertional relapse. Now we have broadened it out because we know that different studies will require different subtypes or overlapping conditions as well. Just call our office or email CFIDS@biobank.org and you'll also get an email response from Gloria Smith, who is our biobank coordinator. We go through a full consent process. The initial part is a registry, so they register all the clinical data, an extensive capture of all the medical history and as much data as the patient has access to, and then as we enroll studies we can make sure we have the right sample at the right time for the study being done. Our hope is that we can expand well beyond the 500 people we have now and include longitudinal data over time so we can do the kind of secondary analysis that Dr. Maier was talking about earlier. We think this is a rich source of discovery as well as validation for other studies that are going on. It is a cost-effective way for both the investigator and the population.

Dr. Dimitrakoff: Is the biobank study registered on ClinicalTrials.gov?

Ms. McCleary: We haven't done that but we should. We're not doing any clinical trials per se. Beth also mentioned the Registry of Registries, for people who may not be aware of it. We have found that there are a lot scientists out there who would like to do research but they have no access to a clinical population and adding on to that an NIH application puts them over the limits of what they would be able to apply for funding-wise. We see this as a great infrastructure support that we can provide and give the patient community a way to participate and galvanize around this kind of research.

Dr. Dimitrakoff: Could you give us more details about the review process of the applications that are being submitted? You mentioned that some of the applications that you funded, but I think it will be helpful for the research community and the people in general who are interested in applying for the grants from CFIDS what the review process involves and what they should expect.

Ms. McCleary: We have a very rigorous review process. For the last two funding opportunities we had, oddly, 37 letters of intent. It was the same number both times. We went through a letter of intent review and in this last round we invited 26 full proposals. It's an application very similar to the NIH RO1 format. We sent those applications that we received out to reviewers within the subject matter. We involved 54 reviewers internationally. We do a second level of review for strategic merit. First, the applications are scored by the peer reviewers on scientific merit—the study design, the question that is being answered, how the population is defined, and all those things. Then we look at the applications from a strategic standpoint—how likely is this to advance our knowledge? Does this fill important gaps? Is this an idea that if brought forward to the NIH as the next stage would be likely to go on and compete well for funding? Then the top proposals are funded. Our pay line is about 20 percent, so we're doing a little bit better than the NIH overall right now. We're hoping that with success in our fundraising, we'll be able to do even better than that. We're very encouraged that out of 37 independent applications for funding, 26 of those were worth bringing in for full proposals. We hope that even at the modest amounts we fund, that pipeline begins to transfer over to what the NIH is doing.

Dr. Dimitrakoff: So you meet Dr. Maier's definition of a successful application: promise of future success.

Dr. Fletcher: How did you develop the criteria for measuring the strategic value of the applications?

Ms. McCleary: The scientific advisory board helped us develop what the criteria would be. Then we looked at some of the gaps out in the literature. We did a whole literature survey to see what the gaps were. Then that decision was made and presented to the executive committee that makes the final funding decisions based on this double review.

Dr. Fletcher: As a long-time feminist, I ask if there was some kind of gender selection of the applications that were funded.

Ms. McCleary: No…you did see a lot of males up there.

Dr. Fletcher: I think they were all male.

Ms. McCleary: In the last round, that was not the case. Maybe Dr. Maier and I should have a conversation about what NIH is doing to diversify the gender gap. In the scientific community, we did have some young investigators. We've had some minority investigators funded, so we're trying to do better on that. But the field is small and we have what we have.

Dr. Dimitrakoff: So it's an opportunity for female investigators.

Ms. McCleary: That's right.

Dr. Dimitrakoff: When is your next round?

Ms. McCleary: We haven't scheduled that yet.

Ms. Holderman: With so much mischaracterization about ME/CFS patients and advocates, so much maligning over the years and stereotyping, I just want to say that this panel today is proof that these are some of the most impressive people who I have ever met. The efforts you're doing and the grace with which you do it is inspiring. I know you don't get to hear that enough. I wanted to say that.

Many concerns are coming from advocates and other groups about not looking in the right places for infectious agents. People want tissue banks so that viral loads can be looked at in the brain and heart and so on. Does your biobank do something like that?

Ms. McCleary: Our IRB approval right now is for blood and *???* tissue. Those are accessible—easy to get at with a needle stick. Tissue samples from organs are more invasive and require unbelievable protocols to make sure that a sample collected in one place and a sample collected in another place would indeed be comparable from a pathology standpoint. There are some barriers for which we don't yet have the resources. We have built the foundation to hopefully expand to that in the future. We've also had many requests from people who would like to indicate in a living will that should they pass, they would have the opportunity to provide samples to the biobank. We are looking into that as something for the future as well. We've looked at some of the Parkinson's and Alzheimer's models out there and the infrastructure they need in order to do the counseling of the family members. It's a major undertaking but it's a very important one. We hope to some day be part of that.

Dr. Vincent: The disease modifying agents, the diseasing modifying strategy that you have—what type of pathogenesis is this directed to? Is it infectious, immune, autonomic?

Ms. McCleary: We are not pursing it based on any one model. We're still making use of the important strength of investigator-initiated ideas about that. If I had the opportunity to talk more about those projects, you would see how each of those investigators is coming at this from a different angle. And then we have the agnostic drug repurposing screening that's using a commercial platform that Biovista has developed to look at mechanisms of actions based on symptomology and 5,000 articles in the literature so far to see what matches they can find. Then we'll do a more careful pruning of that without any real bias starting out from either an allergy infection, neurologic…We're just looking at the whole universe of possibilities, then try to narrow down based on what makes sense in terms of the findings so far of things that looks promising that have come more recently that may not be fully invested in the literature but the knowledge base is building.

Mr. Krafchick: How many samples do you have and do you have good histories on the patients who have given the samples?

Ms. McCleary: We have excellent histories. We have samples in the bank from about 200 of the 500 people that are registered. Those break down into dozens of aliquots. That's how we're able to make that inventory stretch.

Dr. Lee: This has been great and again, I appreciate all five organizations coming here on their own dime. It really helps us.

ME/CFS Case Definition – A Path Forward to Consensus

Dr. Lee: CFSAC has had many discussions over the years about the case definition for CFS. I certainly understand why this is important at many, many levels. I think the entire advisory committee agrees that this is not an issue that we can resolve around this table. There are many disparate thoughts about how to go forward with this just within our small group. I am proposing for us to come up with a working plan on what we can do as a committee to move this forward and where we need to end up. I want you to give me a little leeway for at least a bit to see if we can come up with what I call an action plan to move this particular topic forward so that at the end of our action plan we have what it is we want.

I volunteered to lead this discussion. Marty and I have been working in the Office on Women's Health on a strategic planning process. We are using a specific action planning technique to move our office

forward. I would like to propose that we use this particular method today and come up with some ideas about how we move this forward. I'm thinking that these could be tasks for the subcommittees to take action on over the course of the next months so that this would give some direct tasks and strategies to our two subcommittees. If we need another subcommittee, we can certainly create another subcommittee. That's not really an issue. If this ends up needing a meeting at NIH or CDC, so be it. Marty is going to be helping me with this because we've both been using this process.

The first thing that I would like to get clarified is that at the end of this process of getting a good case definition, what is it that we want to have at the end of the process? What would be the big goal? I think we need to know what that is first. Then we can see how we're going to get there.

Mr. Krafchick: I'm wondering if we can take up the primer first and then go to that—it's a long discussion.

Dr. Lee: We'll take up the primer at 3:30 pm during our discussion of recommendations. I'm just trying to stick to the agenda.

Mr. Krafchick: It would be useful as a CFSAC member to get the agenda and materials ahead of time. Then we get a chance to study them before we walk into the meeting. I would appreciate that. I know it's been done in the past, so I'm hoping we can do it. We had them e-mailed to us a week ahead of time in the past.

Ms. Bond: We did our best to prepare the agenda several weeks in advance, so you did have the agenda.

Mr. Krafchick: I was in trial, so I may have missed the e-mail.

Ms. Bond: We will see what we can do about the materials. Historically, we've had to prepare duplicates because what we send out gets left at the office when people travel.

Mr. Krafchick: If they're sent electronically, then we don't waste paper.

Dr. Lee: The agenda was sent electronically and has been posted for almost two weeks. So, to regroup, what I would like is the goal.

Dr. Levine: I think just based on the last two years when we have been talking about case definitions—Fukuda, the Canadian case definition—we may need two case definitions. We may need a research case definition that is useful where we really have to be careful in terms of characterizing patients for research purposes and then kind of a clinical case definition for clinicians and others who see patients. There's probably going to be a lot of overlap, but in terms of the rigor that we are applying, with each of those, there may be some differences.

Dr. Lee: Is the clinical case definition the one that would apply to things such as Social Security disability?

Dr. Levine: It might apply to that or just getting a diagnosis in a clinical setting or deciding on treatment options. It's probably a little bit more fluid than the research case definition.

Dr. Lee: I remember that Amanda was talking yesterday about Social Security has a definition that they use. I'm just wondering which definition would be used for Social Security, if they use one at all.

Ms. Perry: I can't speak for the SSA, just from my knowledge of it. Generally there is a diagnosis. Case definitions are not really used per se in the Social Security determination process. That would be diagnosis, but then they would evaluate disability based on function.

Dr. Levine: As a clinician, you get caught up in the patient's narrative. It's—for a lack of a better term—your hunch or your best guess that this is what the patient has, based on listening to the story, certain elements coming together, laboratory data, etc. The clinical definition is more fluid and may not meet every single criterion at that moment. The research definition might have to be more rigorous.

Dr. Lee: I remember as a clinician that I would have what I would call clinical definitions of lupus and rheumatoid arthritis that the American College of Rheumatology developed, that all the medical students had, that said if you have three of the five major and six of the seven major...Is that what a clinical definition would be like?

Dr. Levine: Something like that. But as you said, we have seronegative lupus, yet you still feel in your heart that this person has lupus. Just because they're missing a positive result doesn't mean that they don't have it. It gives you a little bit of wiggle room in terms of what your clinical judgment is.

Dr. Vincent: A clinical definition is a little bit different than an algorithm. I think an algorithm leads to a clinical definition. Since 2010, there have been clinical criteria for fibromyalgia, then there are research criteria that are modified from the critical criteria. I'd say we can use that as a model. However, the difference between fibromyalgia and CFS is that FM is not a diagnosis of exclusion. With CFS, the problem that we face in clinical practice—and I'm speaking for myself—is the conclusion regarding exclusionary conditions. It's really difficult. I think the algorithm would help with trying to sort out some of these questions clinicians have. Also, what is the appropriate initial diagnostic work up? I think that's also confusing.

Dr. Lee: I think we may be getting into the discussion. Let me bring us back to what is it that we want to end up with at the end of this process?

Dr. Corbin: From a new member's perspective, in order for me to get my head around what we want at the end of the day, I have to have a better understanding of what the problems are with the current case definitions, so I know what we are trying to change. I know there's dissatisfaction, but can somebody articulate that?

Dr. Dimitrakoff: There are several definitions that people have been talking about in the past couple of days and over the past meetings. There is the 1994 Fukuda definition, which has been used most widely. It's a set of research criteria which have de facto become the clinical criteria for diagnosing CFS. There is a more recent set of criteria—the Canadian criteria—which a lot of people have proposed should be used in lieu of the Fukuda definition. It is difficult to summarize what people have done over the last 20 years in two minutes. I don't know whether that's helpful or not.

At the end of the process , the way that I see it is what would probably be helpful for the clinicians is just having a definition of what ME/CFS really is. I don't think we'll be able to have only that one sentence the way we have it for, say, an acute myocardial infarction, or another condition that's so well defined. I think that we'll probably end up having a sentence defining what ME/CFS is, followed by a set of exclusion criteria. We, as a committee, depending on our discussion, can specify certain number of major and minor criteria.

Dr. Lee: I would like to offer a cautionary note. I don't believe that this committee should be the only people to do this. What I see our role is to lead. We don't have to say who's doing it right now. We need to say we want to get it done and how we get there. I think it would be presumptuous of us to be the

only people to do it. I think our goal is to have a widely accepted definition that is by the clinical community throughout the United States. I think that is a bigger goal—one that gets us further along.

Dr. Dimitrakoff: There should also be a common language about the disease. That should be our goal. When we actually recruit those patients for those studies where we are looking for biomarkers or for treatments, we actually know that we are talking about exactly the same patient rather than different patients or patients with broadly the same condition but maybe different subsets.

Mr. Krafchick: Ann mentioned fibromyalgia and I think that's instructive. In 1990, a group of rheumatologists got together and set up a set of criteria for research purposes. It wasn't very long after that that those became clinical criteria. In practice, the clinical criteria didn't work because they were keyed to tender points. For research, you wanted 11 out of 18, and then somebody would meet it on one day and six months later they would only have seven. Do they still have fibromyalgia? The alternate criteria that were put up abandoned the tender points and made it totally symptom-specific, with a scoring system for several categories of different problems. They divided the body into 19 parts. If you have 7 of 19, then you only need three points. If you have 3 to 6 out of 19, you need 9 points out of the other things.

The issue is broader though, because if it is strictly a self-reported condition, then you begin to enter into the legal world where benefits for disability claims are going to be limited to 24 months instead of age 65. A lot of times when the criteria are thought of, those kinds of things are ignored. If the fibromyalgia community truly has abandoned the tender point exam, they're going to undo 20 years of litigation and take fibromyalgia people and kick them off disability claims because now they're all self-reported because it's all symptom-based. This is something that underlies a lot of the goals. The goals are to have a research definition so that you can study the same patients and at the same time have one that works in clinical practice, and there's the challenge.

Dr. Rose: Is the committee thinking about rehashing the whole definition and reinventing the egg as opposed to picking the Fukuda, the Canadian, or one of the ones that have already been proposed and already been hashed throughout the years by many people?

Dr. Lee: I don't see the committee making this decision.

Dr. Rose: I don't see the committee as having the responsibility of rehashing the egg when people who are involved and have been involved over the years have hashed it.

Dr. Lee: What we have to do, I believe, is come up with a way, just like the American College of Rheumatology came up with a way, to develop definitions for rheumatoid arthritis and lupus well before there were many biomarkers. That was a public/private partnership of some sort. That's what I'm seeing at the end of our process, and so I want to figure out how we get there.

Ms. Holderman: I agree with you Nancy. What about a series of conferences? Two, maybe, or three, or however many you think is needed, where the government sponsors and our clinical partners…It's inclusive. It involves all stakeholders—medical, academic, scientific, private, advocacy—all the communities are there giving input. Whether they decide it's creating a new research definition plus a new clinical definition and reaching consensus and from that point forward, all governments, all private institutions, everybody uses the same thing so we get on the same page about what this disease is and we can begin to replicate studies. If we could sponsor a conference like that, it would be great.

Dr. Lee: To me that's still not the goal. That isn't a goal. I want to come up with the goal.

Ms. Holderman: If you have the conference, wouldn't that be where you accomplish it?

Dr. Lee: Yes, so what is the goal? I want the wording of our goal. What are we striving for?

Ms. Holderman: Is it coming in the form of a recommendation?

Dr. Lee: Not yet.

Dr. Levine: We want to find a way to describe a heterogeneous group of patients to the satisfaction of both clinicians and researchers, but with the caveat that when these biomarkers do become available and they're replicated and prove they're reliable, we can add the biomarker as a feature of our case definition.

Dr. Lee: Is our ultimate goal here to have case definitions that are suitable for research and for clinical use that are widely accepted by many types of providers and insurers and whatever around the country? Is that a goal people could get their arm around? [CFSAC members indicate that they could support the goal.]

The next thing is, how do we get there? Terry and I had a great conversation. Could you please talk about how can we learn from other disease entities in this process?

Dr. Michele: Sure. First, I want to compliment Dr. Levine because she hit the nail on the head. Research definitions are sometimes more restrictive than patient definitions. A common example: COPD [chronic obstructive pulmonary disease]. People think they know what it is, though I'm not too sure. Every clinical trial of COPD requires you to meet specific pulmonary function tests as criteria. However, I can tell you I see patients in clinic every week who don't necessarily meet those criteria, but they do have COPD. They also may have other comorbid illnesses that mess up their pulmonary function tests. That's just one example, but I think it fits in a heterogeneous disease like this even more so. With that said, we have to be very careful with our research studies or we'll end up with a mess again, which doesn't help anybody.

The question is, how do you get to a research definition so that you have the basis to proceed with drug trials with confidence that you're all looking at the same thing? Nancy asked me how the FDA defines a new disease. The FDA doesn't define a new disease. What happens is that the community—and I'm being very inclusive here—defines the disease. Typically, there are consensus panels by some of the physician groups. The American Thoracic Society or the American Rheumatology Society and so forth.

In this case, we are kind of at a disadvantage because this disease doesn't quite have a medical home. I think that to begin to build consensus around these things we need to think about being inclusive of some of the physician specialty groups that might have an impact on this disease and be very inclusive of them so that when more consensus is reached, and maybe not reinventing the wheel. Maybe the consensus is around something that is already out there but it's accepted very broadly. Once there is broad acceptance, the FDA can look at that and we can incorporate the ideas that work [in?] research as part of our guidance document. Typically, our guidance documents are based on the consensus that's out in the field.

An example is idiopathic pulmonary fibrosis. Recently there's an effort to try to define endpoints for that disease. That's another horrible, awful disease…lung disease where people die in about three years. The problem is how do you define endpoints for that? We don't really know. So they came to us and said, "What endpoints should we use?" We had some ideas, but what happened was a physician group in the American Thoracic Society got together and worked on endpoints in a very inclusive way and published a paper on it. We can go out to pharmaceutical companies and say, "Look at this. This is what's out in the field." There are ways to get things moving forward. I totally agree with Nancy's ideas as well as what you said, that we need to be inclusive. We particularly need to engage the physician society groups because until you've done that, there's still going to be this fringe stuff that nobody quite agrees with.

Dr. Dimitrakoff: Another example of a process like this the MAP Network—the multidisciplinary approach to CFS that was sponsored by NIH. I think that discussion has been ongoing for four years, so I don't think it will only take a conference or two to be able to do that if you're really trying to be inclusive.

Dr. Michele: That may be a kick start, but I totally agree with you. This is not going to be a one-shot deal, come out at the end of a conference and be done. We're still probably going to be talking about this 20 years from now because our understanding of the disease is going to evolve. I can tell you that we've known about COPD for a very long time and physicians are still talking about, "How do we better define this in research? How do we define subpopulations?" There's a huge NIH-sponsored study going on looking at exactly that to facilitate drug development. This is kind of like cleaning your house. It's one of those things that's never done, but you get to a better stage: a stage of improvement.

Dr. Sharp: So, a conference or set of conferences is one way to get to the goal. I'm trying to be 21st century and think about there are perhaps some more modern mechanisms where we could have discussions. Perhaps Phoenix Rising or other groups could give us advice on web-based discussions. That might be another path to the end and perhaps faster than conferences once a year.

Ms. Holderman: I agree with everything you said and I do agree that it will be an ongoing process and we'll always be refining the definition. But what is so concerning to patients is decade after decade. It's almost one step forward, two steps back. Not to rehash or pick on the CDC, but with the empirical definition and things like that that come along, it does set us back. So there is an urgency to attend to this. We want to move forward and even if moving forward takes ten years, as long as it's moving forward without steps back, I'm cool with that.

Dr. Belay: Just to discredit a myth, the CDC case definition and the other variation that came out were not designed for clinical practice. I think everybody should understand that. It was designed specifically for epidemiologic research. No one believes that physicians should wait for six months, for example, before they start treating patients. You have to draw a line somewhere for epidemiologic research and that's what was done. Is it a perfect case definition? Anybody could argue on that. Personally I think it will be very challenging to get one simple bullet case definition for CFS. Always there is a give-and-take for sensitivity and specificity. That will be our challenge going forward.

Dr. Lee: We shouldn't stop because of that kind of difficulty. We should come forward with it. I think lupus is a great model.

Dr. Belay: There are two points I wanted to make. One is that it's always important to involve the physicians associations when developing definitions. If we are intending for physicians to use them, we have to create a situation where the physicians will have buy-in. One of the ways to do that is involving the physician association groups. My second point is that I think the definitions should be data-driven. We should not be creating a case definition in a vacuum. It has to be supported by data. That's one of the reasons we started the project in the seven clinics. We're going to the physicians in those seven clinics and we're asking them to use their best judgment—not any one case definition—but to use their best judgment to diagnose a patient with CFS and collect as many data as possible to help us in trying to characterize the heterogeneity of the disease from those multiple sites. I believe data like that should inform the discussions that we have in the future.

Dr. Maier: I see a parallel here in the history of this particular illness with respect to another one I did research for a number of years and that's fetal alcohol syndrome. It started out being defined more than 30 years ago with a very specific set of criteria, very specific indicators: no biomarkers, no tests except for very specific ones that weren't case definition criteria. The problem as the field developed and so the clinicians kept seeing these kids and they would talk to the animal researchers and basic research

scientists and say here's what the kids do. Can you model this? The animal people would model that and take it back and say "can you use these types of therapies with the children," so there was this feedback. The feedback eventually led to a reclassification: a redefinition that is now fetal alcohol spectrum disorder because it added additional things that are required for the definition because what was happening was the children who did not quite have fetal alcohol syndrome by definition were missing out on critical services. That led to a further refinement, even though it was a broadening of the category, a refinement of the research to advance that field. This field has moved much faster in the last 10 years than it did in the previous 20.

Dr. Lee: I would like to ask, would another part of the goal be that we have a different name?

Ms. Holerman: The name change is one of the hottest issues for the patient community. Everyone's concerned about it for many, many reasons.

Dr. Lee: Would you want to make that a goal?

Ms. Holderman: That would be a great goal.

Dr. Lee: You can only get what you wish for and put down on paper. I don't know whether that's too hard to get at the same time as you get the case definition, but you can always think about it.

Ms. Holderman: They are tied in. Those are things that are tied in—ICD, name change, case definition. They're all interwoven. It would be, I think, an appropriate time to have that dialog and really consider getting the name changed.

Dr. Vincent: I think a data-driven, well-characterized case definition with the right name would also take out a lot of stigma that patients face and the provider community faces.

Dr. Lee: These are all really good suggestions. I think this is framing in context. So how do we get there? How do we as a group of just a few people get there? What can we do as a committee?

Mr. Krafchick: We read Lenny Jason's article and looked at it carefully because he proposes an ME definition. Unfortunately, the one in our packets is every other page. I printed out a full one.

Dr. Lee: That's one step. So, how do we get to getting to a definition? I don't think we just want to advocate for Lenny's definition. We can't do this without the physician and other provider community. They have got to have buy-in here. Definitely, Lenny's paper is part of it.

Mr. Krafchick: It's a very good history of the development of the different criteria and a comparison of the different criteria, along with a proposal that probably would function pretty well today. I raise it in that context. It's a process and even if we would recommend something like this today or next year or whenever we choose to do it, that doesn't mean that there isn't going to be more discussion about it and more change in it. The problem is that somebody's just got to grab the bull by the horns and do something.

Dr. Lee: That's what I'm trying to do, so what will we do in the next three weeks, in the next three months, in the next six months in the subcommittees? We have subcommittees; we can get action.

Ms. Perry: I just want to raise one question in regard to the process. I really appreciate the points that Ermias and Theresa made about bringing in some of the physician groups and getting that buy-in. The challenge with that is the learning curve. Those groups that we want to help bring to consensus are the same groups that we're talking about sending the primer out to because they don't have much knowledge

of this. I'm not saying that's a reason not to bring them in. I'm just saying that's one of the things we need to think about when we're thinking about process.

Dr. Lee: We're doing something like this in our office around screening for interpersonal violence. We are organizing a meeting and writing the letter right now for the big primary care providers to come to learn about how one screens for interpersonal violence in a primary care clinic setting. You just go and you educate the leadership of each of those physician groups and then you start working with them.

Dr. Dimitrakoff: I think the way to go to get to the goal in the way at least I understand it is for us to recommend that we initiate this process engaging the different physician organizations. The way we can do that is to [have?] an ongoing discussion that doesn't have to be happening only twice a year. We should set goals and definite time points, at which there should be progress reports or evaluations. At least, let's say, every three months, and definitely every meeting of the CFSAC committee twice a year.

Dr. Fletcher: I can tell you there have been hundreds of committee meetings about the name change stretching back year after year after year. I've never been in one in which anyone really thought that CFS was a good name. If this group has any meaning at all, I personally think that we should recommend that the name be changed to ME. What happens to that after we make a recommendation, I'm not sure. It doesn't seem to be very fruitful. At least we've done what our only choice is: to make a recommendation.

Mr. Krafchick: I would second that.

Dr. Lee: I personally think we have more in our toolbox than that. To me, the most important thing is the case definition and I believe that the name can fall from there. I get e-mails all the time and one of the big ones that I keep getting is, "Do not put ME in there. It's different than CFS." Is that the best name? I don't know if that's the best name or not. That would be my advice. You all are able to recommend whatever you want. I can't vote. You can make the recommendation, but I personally think that the name would come along with the case definition and that could be a process in which we involve more than just the few of us around the table.

Dr. Levine: We could ask the clinical experts what they feel should be the main criteria of a case definition. Try to poll as many experts as we can internationally and try to come up with a consensus that way.

Mr. Krafchick: I know that as long as I've been sitting on this committee and in the 20 years that I've been working with CFS patients, it's just been a very difficult issue. I feel like I'm a clone of Lenny right now, but he has a case definition for ME and a very well set-up set of criteria. The question I would have is, "Is this an acceptable approach?" Rather than say, "What do you think it should be?" let's start with something tangible and send that out for review and concerns. If we start out with, "What should it be?" we're setting everything back 20 years.

Dr. Lee: It's sort of a straw man that you can put up.

Mr. Krafchick: Exactly.

Dr. Lee: I think that's a great idea.

Dr. Rose: That's my reason for saying let's look at the most favorable criteria so far, which is the Canadian. I thought the issue between the Fukuda and any other definition is that you want to exclude patients with depression being included in patients being defined with CFS. You want to separate the depressed patients from the patients who have ME and that was the issue and the Canadian criteria emphasized post exertional malaise, which would allow for that definition. Rather than go back and start

all, all over again and waste time, start with something that does that to some degree already, which would be the Canadian, or, I'm not against starting with this template. But to start from absolute scratch all, all over again in a disease that isn't settled with a specialty—there's no one specialty that owns it—it's going to be hard to gather the "experts" to come up cold with criteria. We have things to start with rather than rehash all over again and end up 20 years behind. The reason for having a case definition is so we can start having meaningful research. If we can't have meaningful research, we won't progress. It's true, the definition may change over time. All disease definitions change over time. If you don't start with some meaningful research now, you won't be able to find those changes over time.

Ms. Holderman: I basically agree with Steve and Jacqueline. We could have this series of conferences. The invited guests would be very inclusive from all stakeholders, and we could start with a template because a lot of work has been done on this—Lenny Jason's work, the Canadian Consensus criteria, ICC—and we can work from that and tease out what we want. I think that would be a good start.

Dr. Lee: What are our steps to get it so that it's widely accepted around the country?

Ms. Holderman: Would that be discussed at the conferences?

Dr. Michele: I think we're missing steps here. We're jumping to the end. Let me back up a little bit and frame what I think I'm hearing. We talked about engaging physician groups. I think one of our subcommittees has to take [that] on as the goal for next time to try to figure out how we engage those physician groups and come up with a plan for that.

The second thing that we need to come up with a plan for is a list of the data to be considered because in order for this to be a useful exercise at the end of the day for clinical trials, it has to be a data-driven exercise. It can't be what someone feels the criteria should be. We have to figure out what data we are going to use to drive the exercise. It may be that we don't have all that data yet, but we know where it's coming from. Another subcommittee exercise could be to figure out a list of the data that we're going to use to drive this.

A third piece that we need to come up with, I think we've heard very strongly from the group, that we have a number of definitions floating out there and we need to figure out which of them we are going to put forward for consideration in this data-driven exercise. Once we have those three pieces in place, then we have the makings of a conference that could begin to work on this process. Things always work better face-to-face in terms of starting a process, but then we can use the suggestions to make the process go forward, perhaps by using a web-driven or some other mechanism that is not quite as labor- and dollar-intensive to move the process forward because there will be a lot of work taking that data, applying it, and figuring out what's going to work best in a research project. At the end of the day, you come up with something that hopefully, because all of these groups have worked on it, you have some consensus in what people are going to use doing research.

As a side effect, we may come up with a couple of good things. We may come up with a new name if we have that at the back of our minds, and more importantly, we may get some other researchers excited about this. If we're engaging the societies and they're actively putting resources into coming up with definitions, they are going to want to use them. Wouldn't that be great?

Dr. Lee: One of the things that I would like by the next meeting is to have our subcommittees already have started reaching out. I think we have plenty of time. I think it's probably a good idea to use both subcommittees because we have clinicians on both subcommittees and other people who have contacts and affiliations with various and sundry groups. We could give people tasks to meet with their leadership. Much of the leadership for clinical physician groups are here in D.C. and Chicago and New

York. They are in a few locations. We could also use our colleagues on the other side of the table. They can begin reaching out. But we need to have a coordinated plan.

Mr. Krafchick: If we're going to reach out, I propose that we start with the ME definition that is proposed in Jason's article as a starting point. That's what we reach out with, get feedback on that, work off that, because otherwise it's too mushy. When I read his article, he convinced me that his definition is better than the Canadian one, rightly or wrongly. We could pick the Canadian one and do it. It's some place to start that's more tangible than nothing.

Dr. Lee: Or go to these groups and educate them. We have already heard that there is a lot of misinformation, even among the leadership of these primary care groups around CFS. So educate them to the problem and to our goal of coming up with a good, useful definition.

Mr. Krafchick: One doesn't exclude the other. The problem is unless we pick one to start with and to talk about as our starting point, we're not going to do any better than what has been done the last 10 or 15 years.

Dr. Fletcher: We're leaving out one group, and that's the IACFS/ME. It's an international association of researchers in CFS/ME.

Dr. Lee: They were invited but were not able to come today.

Dr. Fletcher: That group is the most knowledgeable. I can tell you that the American Medical Association is not going to be particularly…

Dr. Lee: To get this to be used widely around the country, isn't that the very sort of groups we've got to get?

Dr. Fletcher: I don't think you'll ever get them.

Dr. Lee: Can't get them if we don't start trying.

Dr. Rose: I think it's important that the criteria be accurate and be scientifically based and people who haven't been working on it, how are they going to weigh in on a criterion when they're not the experts on it and they haven't been working in it? You get all the stakeholders and if the stakeholders don't know anything, how can they add anything informative if they haven't been working with the problem. If they haven't been involved in it or had experience in it. How are they going to contribute to the criteria?

Dr. Lee: The thing that Susan started off with was two definitions. So we have the research definition and we have the clinical definition. I hear over and over again how people with ME/CFS go through many physicians before they find one who can figure it out. So we need to get the primary care physicians on board for at least the clinical definition. I think that we have to bring some of those people to the table.

Ms. Perry: What you're saying is echoing the Catch-22 that I had raised. I completely understand the importance of buy-in. At the same time, to ask people who know nothing about the condition to weigh in on a case definition for a condition that they're not familiar with.

Dr. Lee: So maybe there are two meetings. There's the meeting where we come up with a case definition and then we have another conference where we bring representatives from the clinical community to educate them and get their input.

Dr. Cook: I want to go on record as saying that I'm against reinventing the wheel, but I'd like to ask Ermias and Theresa what they mean by it has to be data-driven. There are many case definitions out there. I don't think it's a good use of the committee's time to create a new one. Your comment suggested that we're going to go and try to get consensus on a definition.

Dr. Belay: I think any case definition—existing or new—should be able to be backed up by data that would, for example, try to calculate the specificity of that particular case definition compared to what a physician diagnoses. In other words, we should have some sets of parameters for you to be able to evaluate.

Dr. Cook: Are we going backwards to look at old data or are we going forward and collecting new data?

Dr. Belay: It could be either one as long as that data is useful.

Dr. Cook: If we go forward in collecting new data, we're talking a very long process. If we go backwards to look at old data, all we're doing is looking at the Fukuda case definition. That is the only criteria that has been used in 99 percent of the research.

Dr. Belay: When I say data, a good example I could use is the data that we're collecting in the seven clinics. The data that's being collected in the seven clinics does not specify any case definition. It's just the best judgment of physicians who have treated CFS patients for years and years using their best judgment. What are the cases that they would classify as having CFS in collecting as many parameters as possible that would allow us then to apply to those case definitions and see how those case definitions would compare.

Dr. Cook: To me, this prospective approach is the most powerful way to go.

Dr. Rose: When will those data be ready?

Dr. Belay: They have started collecting the data, but I can't give you a date because it's dependent on those physicians, not us at CDC. Some of the sites have already started enrolling patients and we're shooting for about 400 patients eventually to be enrolled. If that happens within the next 16 to 18 months, that will be great.

Dr. Cook: Do you see the limitation that I saw by our initial conversation is that if we look backwards as Lenny's work has done, and the big limitation is that all the studies and all the research that they're basing the definition on used the Fukuda criteria for the entry criteria for all the patients. It's totally flawed to then try to say this is an ME group versus a CFS group versus an ME plus CFS group or whatever. It's very limited. But a prospective way that is blind to that doesn't subscribe to a certain definition upfront and then apply criteria. That is the way that is less limited.

Mr. Krafchick: The problem is that you still have to identify the patients ahead of time.

Dr. Fletcher: What definition did you use?

Dr. Belay: We are using the best judgment.

Mr. Krafchick: So there are no criteria. That's not going to work real well.

Dr. Lee: It might work. These are researchers who have been thinking about this for 25 years. Nancy Klimas is one of the researchers.

Dr. Fletcher: I don't think she intended it to result in a new case definition.

Dr. Lee: So should we just give this up and not worry about a new case definition?

Ms. Holderman: At the five centers, did you say to the investigators, "Collect the data and the data set is up to you to use whatever criteria is out there? Are they naming the criteria?

Dr. Belay: We basically left it to them to make that decision using their best judgment. We don't want to box them in to a case definition.

Dr. Levine: Do think they'll be able to go back to how they made that decision and say I used such and such criteria?

Dr. Belay: They should be able to.

Dr. Lee: Fukuda was a research definition and this is a clinical study.

Ms. Holderman: So in other words, do they know what criteria they're using or are they blending them?

Dr. Belay: We have to trust physicians at one point. These are physicians who have a lot of experience. They have been treating ME/CFS for years and years and years. For example, we have Dr. Klimas and Dr. Klimas sees from her judgment and her practice, using whatever criteria she uses, that a particular patient is a CFS patient. We're going to use him or her in the study.

Dr. Fletcher: I can tell you for sure what Nancy Klimas uses on all patients put into a research study. Now she uses the Canadian. Before that she used Fukuda. And I can also say that Reeves did a lot of damage when he at the CDC made that revision of the Fukuda that opened up the case definition to a whole lot of people with depression. We have to be really careful about this kind of thing.

Dr. Lee: It may be that it is not the research definition that Dr. Klimas is using but who she is treating for CFS in her practice and who she says, to the patient, you have CFS.

Dr. Fletcher: That's what she uses to say that to them. She wouldn't want to say to a patient that you have CFS if they didn't meet some definition.

Dr. Dimitrakoff: There is a lot of value and merit in the study that the CDC is doing. I don't work for the CDC but the way I understand it is that you actually asked people, using their best judgment, to say whether someone has or doesn't have CFS/ME and then they still collect a uniform set of symptoms from those patients, which eventually you want to use in a data-driven approach to go back and say for all those seven centers, the core symptoms that characterize this condition are fatigue, this and this and this and then redefine the disease. I think that's what we're actually trying to accomplish.

Ms. Holderman: So you're not asking the investigators of those five places to decide what kind of criteria they're using. You're saying pick your patients, collect their symptoms, and never reveal what criteria you based it on?

Dr. Levine: I guess at the end of the study they're going to reveal it.

Ms. Holderman: They do know what criteria they're using, right?

Dr. Belay: Of course.

Dr. Lee: This is a big issue. We only had an hour for it and we took a little more than an hour. I think that what we need to do is continue this discussion over the phone. What I may do is propose some action steps for the subcommittees and we'll see what people think.

Dr. Levine: Do we have access to the 780 set? It would be interesting to know which providers bill to Medicare with the CF code. Would we be able to tell whether they are primary care providers or specialists? You said there was some kind of coding data available to us.

Ms. Perry: Getting into that level of specificity in the date might be very challenging. I don't know for sure. If we look back and use old data, I think we run into the issue that Dane raised.

Mr. Krafchick: I think what the CDC is doing is the right way to go about it because fibromyalgia started out…T hey got a bunch of people who were diagnosed with fibromyalgia and they collected information about them, and then they looked at the data to figure out what were the commonalities and figured out diagnostic criteria. If I criticized you earlier, I take it back. But I still think we have to start with something to go forward with.

Committee Discussion: Finalize Recommendations

CFS Primer

Dr. Lee: Dr. Cook was the cautionary person who said we should all read it first.

Mr. Krafchick: I have no objections to people being well-informed. I did look up the primer on the IACFS/ME website and found two things. First, they ask you to make a little donation but it's not required, and second, in their terms of use, they say they want the primer widely distributed.

My motion would be to recommend that this primer be adopted in lieu of the toolkit by the CDC, providing we get agreement from the IACFS/ME, from the authors, or from whoever is appropriate, and that we work to widely distribute this primer to the primary care physicians.

Dr. Fletcher seconded the motion.

Dr. Willis-Fillinger: We want to engage as many primary care providers and others as possible in caring for patients with this disorder. That said, traditionally on the government's side, as obstructive as it may appear to some, we also defer to professional societies and health professional organizations to determine care and treatment algorithms and patterns. The government doesn't dictate that to healthcare providers.

In some cases, we support guidelines development. We bring expert clinicians together and let them hash it out. They tell us what they want to do and we say thank you. It's engaging health professionals in a longitudinal educational process over time where we're bringing them to the table to hash out their best approach to whatever it is and to look at the data that we have before us with their recommendations. I'm going to try to figure out as a clinician how to use the primer, but when it comes to the government distributing and endorsing something, that's a little more difficult. That's why we're here, to figure it out together.

Mr. Krafchick: I wasn't suggesting that the government go to the print shop and print a million copies of this. How it's distributed and where it's distributed is not necessarily our decision here. It is a good, basic document that gives a primary care physician a real road map, whether it is to consider a differential diagnosis or different treatment options. There's nothing like it anywhere else. There have been concerns

about the toolkit. Dr. Belay is in the process of rewriting it, but with all due respect to the CDC, I don't know if they can do a much better job than the primer. That's why I make the proposal.

Dr. Lee: There's a problem that we have in the federal government in general about seemingly endorsing one thing over something else that is not produced by ourselves. Guidelines.gov is something from AHRQ that puts everybody's guidelines out there. That's a way that we can link as a federal agency to outside guidelines.

Dr. Collins Sharp: That's a good point, Nancy, because I'm sitting here getting very nervous about how this would likely be unsuccessful—a non-starter, actually—for the government to be able to endorse the primer.

Mr. Krafchick: We're an advisory committee. Can't we endorse it and recommend that the government implement it?

Dr. Collins Sharp: But then we'll be unsuccessful, and at the next meeting you'll come and criticize that we didn't do that because we're not able to that. You can endorse it, but we can't implement it, or enforce it, or regulate it.

Mr. Krafchick: Unless the CDC adopted it as their toolkit.

Dr. Collins Sharp: And in order to do that—I shouldn't speak on behalf of the CDC—but in order to do that there would be a lengthy review and clearance process. Guidelines.gov is a nice idea. It is a clearinghouse for clinical guidelines. There's also one for innovations and one for quality measures. It is a clearinghouse where guidelines are posted. The nice thing about Guidelines.gov is that there's an independent editorial board and a standard for the quality of guidelines. In order to be listed there you would have to meet quality standards, so that when you go to look for guidelines or clinical guidance, you can be assured that there is a standard of quality.

Dr. Lee: There is a very nice search function and comparison function.

Mr. Krafchick: What's the process?

Dr. Collins Sharp: The IACFS/ME would submit this document.

Mr. Krafchick: Why can't we submit it?

Dr. Collins Sharp: The authors should do that. They own it.

Mr. Krafchick: No, they publish it. In the legal world, when somebody says you can download a document and print it and says that "we want it widely distributed," they have no copyright at all.

Dr. Lee: This committee could recommend that this document be included in Guidelines.gov.

Mr. Krafchick: The recommendation that I would like to make is that the Secretary authorize the appropriate person in HHS to work with the IACFS/ME to make this widely available to primary care providers.

Dr. Fletcher: In the HIV world, someone made a decision about what constituted HIV infection and what constituted AIDS. Was that the government?

Dr. Lee: Knowing how the government works, it was probably some of the government, and then they took the people who were taking care of people with AIDS around the country and around the world and brought them in. I don't know the answer to your question, but knowing how the government works, they wouldn't have done it alone. There aren't a lot of clinicians who work for the government. We don't have a lot of patients, and so we would work with people to develop a definition.

Dr. Willis-Fillinger: We engage the medical community and the clinical societies that are involved and get their best knowledge. It would have involved a lot of clinicians who were actually doing hands-on patient care at the time, pooling their best knowledge together. That's what the IACFS/ME is—the clinical community that's engaged and involved with care of patients with CFS. Traditionally, the approach is to bring as many people to the table as possible and have the conversation. As I explained earlier, with HIV we had a lot of political pressure to act quickly because people were dying. Over a number of years there were clinicians who were actually caring for patients and sharing information about what they were seeing in real time to learn as quickly as possible what would work and what wouldn't work.

Mr. Krafchick: We're not talking about the case definition. We're talking about a primer that can help primary care physicians care for these patients almost immediately.

Dr. Lee: I have a motion on the table to authorize the appropriate person within HHS to work with IACFS/ME to make the primer widely available, particularly to primary care providers.

Dr. Rose: The primer is excellent. It really should be a chapter in Harrison's Internal Medicine text. I have a question about the treatments. For treatment of ME, there aren't a whole lot of studies and evidence. One statement is made that ImmuniVir may be helpful in selected patients, but there's no reference to a study. It just says that a specialist's advice may be in order and that clinical experience is limited. Everybody's clinical experience is going to be limited because I could probably name on one hand the number of people using ImmuniVir. The same thing is true for some supplements and other recommendations. There isn't a series of replicated studies to show benefit with those treatments. Should treatments be recommended in this detail on an official site recommended by the government?

Dr. Lee: We have great difficulty with that sort of thing, but that's the beauty of Guidelines.gov. It serves a different purpose. To go on our website or CDC's would be more problematic, which is why Beth called it a non-starter.

Dr. Cook: Jacqueline brings up a good point. Is it possible for us to meet in subcommittees, review the primer, and make recommendations to IACFS/ME on modifications to it before we fully endorse it?

Dr. Fletcher: The way I read it is that some physicians use those substances. It doesn't mean that they're recommended. In fact, it says that you should seek expert advice for doing it.

Dr. Cook: That's one interpretation of that, but you can also criticize them for not providing more detail on that. If they're unable to, that's fine.

Dr. Fletcher: It's going to end up in the document not being circulated in a timely way.

Dr. Cook: I disagree. I think the subcommittees could get together. We've all worked well together in the past. Maybe we won't come up with anything important enough to make recommendations at all, but I read it twice now, and I came up with new things the second time.

Ms. Perry: It does say the 2012 edition, which to me implies that there could be a 2013 or a 2014, as they said it would be updated on a regular basis. To me is seems that it could be possible for CFSAC to

endorse dissemination of the current version without fully endorsing the complete content. The committee could decide that this is worth disseminating at this point and then perhaps make recommendations for further changes for a future edition.

Dr. Cook: I think that's a good solution.

Mr. Krafchick: My goal is to get this out so that primary care providers can have more information to understand CFS. This is the best thing I've seen in years to do that. I am not a clinician. As sure as we're sitting here, there are going to be changes to this. But I think the message ought to be and the recommendation is, from my perspective, to have this circulated to primary care physicians and to work with the IACFS/ME or the authors or whoever we have to work with to help facilitate that. If facilitating that means that it should be on Guidelines.gov, great. If it means that we should send it to the heads of the different organizations to distribute to their members on behalf of IACFS/ME or CFSAC, great. It's not the be-all and end-all, but it sure is a great beginning.

Dr. Collins Sharp: Thank you for that clarification, because it's helpful. Initially the recommendation sounded a little more prescriptive than I'm understanding it to be now.

Dr. Lee called for a vote on the recommendation:

Recommendation 1

CFSAC recommends that the HHS Secretary authorize the appropriate person within HHS to work with IACFS/ME to make the primer widely available, particularly to primary care providers.

Dr. Lee clarified for **Ms. Holderman** that the phrase "particularly primary care providers" means that they are the first target audience. The phrase is not meant to be exclusionary, and specialties can be added in the future.

The motion passed with one abstention. Dr. Corbin abstained from voting because she had not read the document.

Ms. Holderman presented two recommendations on behalf of **Dr. Levine**, who left the meeting early.

The first recommendation was to place a link on the CFSAC website to the Department of Education's Parent Technical Assistance Center Network. Dr. Lee applauded the recommendation and said that the link could go up in as little as a week.

The second recommendation was to add links to the CFSAC website to patient advocacy organizations, including those that spoke earlier in the day. Dr. Lee cautioned against the appearance of showing favoritism among the groups.

Mr. Krafchick suggested a friendly amendment to develop a list of advocacy organizations to post on the website. Dr. Lee said that her office had been thinking about this issue for some time, including how to be fair and inclusive. She said her office gets questions periodically from people seeking help, and referring them to a list of organizations would be convenient. She added, however, that there have been issues concerning who CFSAC can and cannot link to. More exploration is needed, she concluded. Mr. Krafchick asked that Dr. Lee provide an update on the issue at the next CFSAC meeting and she agreed to do so, noting that more information may be available before then.

Mr. Krafchick then offered a friendly amendment to the recommendation. We recommend that the Secretary authorize people to develop a list of advocacy organizations that can be posted on the CFSAC website.

Dr. Lee suggested that the committee vote on the recommendations in the order Ms. Holderman introduced them. Dr. Lee presented Ms. Holderman's recommendation for a vote. Mr. Krafchick seconded the motion:

Recommendation 2

CFSAC recommends that a link be put on the CFSAC website to the Department of Education's Parent Technical Assistance Center Network (www.talliance.org).

The recommendation passed unanimously.

CFSAC members then discussed the recommendation to add links on the CFSAC website to patient advocacy organizations. Issues discussed included:

- How to develop an inclusive list
- Who should develop that list (HHS staff, CFSAC subcommittees)
- What criteria should be used to decide if a group should be included on the list
- Whether the CFSAC website can post links or only a list of the organizations

Mr. Krafchick suggested that a list be developed as a first step before the committee addresses other issues. Dr. Corbin agreed that CFSAC could make a recommendation to develop a list, then develop a process for determining all the steps necessary for deciding whether or not a group would be included on that list. She added that while someone can do a Google search for relevant groups, it would be nice to have an official organization that people trust list groups that are reliable. Dr. Lee noted that she gets numerous requests for such information in her CFSAC mailbox and a list would be helpful.

Mr. Krafchick seconded Ms. Holderman's motion.

Recommendation 3

CFSAC recommends that HHS staff work with CFSAC members to develop a list of ME/CFS organizations and criteria for posting this list on the CFSAC website.

The motion passed unanimously.

Dr. Dimitrakoff offered a recommendation from the CFSAC Research Subcommittee based on the morning's discussion of biomarkers. The Research Subcommittee recommended that CFSAC put together a white paper on biomarker definition for ME/CFS that can be used for future clinical trials with treatment outcomes.

CFSAC members paused in their discussion to hear testimony from a person who did not get to testify during the scheduled public session.

Loretta Vann

Ms. Holderman: I looked at past CFSAC recommendations and there were about six related to pediatric ME/CFS and/or education. I don't remember seeing one that involved a concerted effort to educate our

educators. That seemed to be a big problem for the parents and kids we talked to yesterday. So many of their ongoing problems would be nipped in the bud if their teachers, nurses, and guidance counselors would be educated on this disease. We could make a recommendation that involves getting the information out to the schools.

Dr. Lee: I can tell you that while the Department of Education and school systems are not the most common of the partners that HHS deals with, they do partner. My particular experience has been at CDC where they had cooperative agreements with every state Department of Education around HIV education. HHS does have experience in partnering with the federal and state Departments of Education.

Dr. Corbin: If I recall, one of the patient advocacy groups was preparing something that would go out to school nurses. The recommendation may be that we endorse that group's work and use connections with the Department of Education to help with distribution.

Ms. Holderman: Does HHS partner with advocacy organizations?

Dr. Lee: CFSAC members can endorse what they want to endorse. HHS can't endorse it.

Dr. Willis-Fillinger: I think your recommendation is a good one if you recommend that HHS partner with the Department of Education to provide information or education for teachers, nurses, and others. I think that would be broad enough and not be prescriptive about the "how."

Dr. Fletcher: We might seek guidance from people who deal with autism. They have had a lot of experience in changing the educational environment for children with autism.

Mary Dimmock: The primer would provide medical specificity to support families.

Ms. Holderman: New Jersey CFIDS is preparing a fact sheet and they've done very successful fact sheets. What do we think educators would read and respond to—a lengthier document or a fact sheet? What would be most helpful?

Dr. Dimitrakoff: A fact sheet is good, but it would be helpful to have the primer for documentation.

Dr. Lee: I think that keeping the recommendation broad is the right way to go. We are already talking about it with the Administration for Children and Families in our Ad Hoc HHS Workgroup. I recall from yesterday that Dr. Houle conveyed the message that "I am here to work with you." I think there are many opportunities and it would be unnecessary to get too specific.

Ms. Holderman: The timing of the toolkit is a problem because so many of them recently went out and the revisions won't begin until 2013. We do one really good thing like disseminate good information, while at the same time information that is not good almost cancels it out. But I don't think that should bar us. We haven't made any official recommendations about the CDC website yet. Dr. Mike Miller suggested that the best way to go about it is the way we are doing it in the review panel, but I also know that we could make a recommendation to the Secretary to remove the toolkit, or consider removing the toolkit, before 2013. We talked about replacing the toolkit with the primer, but Dr. Collins Sharp called it a non-starter.

Dr. Lee: The decisions about what does and does not get posted are way above my pay grade. You can make a recommendation for whatever you like. The government is very careful that what they present is objective, verifiable, and evidence-based. If the government didn't write it, then they have to go back and review it. I think it's a great process. It helps many people very often. That's why we have Guidelines.gov.

Ms. Perry: It sounds like what people are saying is that the primer could not be placed on the CDC website in place of the toolkit. That sounds pretty clear. The question is, does there have to be a document there at all on the CDC website? Could the primer serve the educational purpose? Does there need to be a document like that on the CDC website?

Dr. Belay: The toolkit filled a vacuum. There was no information that was available for physicians at the time. We were filling a gap. Is it complete? It is not complete. Does it educate people about CFS? It does. It has done so many times. We have gotten a lot of positive feedback. The language content could be changed and we've already gotten input from Eileen on that. We've gotten input from others also. The other thing that I am hearing is that the toolkit is not needed because the primer is more detailed and more informative. I'll take that information back to the CDC.

Mr. Krafchick: If taking the toolkit off would help people, it would be good that we recommend that CDC take it off for now.

Dr. Lee: You can make that recommendation.

Ms. Holderman: So Ermias, you would take that information back to the CDC and report back to us without us having to make a formal recommendation that the toolkit be removed?

Dr. Belay: That's correct.

Mr. Krafchick: Well, then, that's not a non-starter for us to recommend if it's going to happen anyway.

Ms. Holderman: He's just taking the idea back. It's not guaranteed to happen.

Mr. Krafchick: I understand that. I would make the recommendation that we ask the Secretary to ask the CDC to take down the toolkit.

Dr. Fletcher seconded the motion.

Recommendation 4

CFSAC recommends that the Secretary asks the CDC to take the toolkit down off the website.

The recommendation passed with one "no" vote from Dr. Corbin.

Ms. Holderman presented the following recommendation;

Recommendation 5

CFSAC recommends that the HHS partner with CFSAC and the Department of Education to educate educators and school nurses on ME/CFS affecting children and adolescents.

Ms. Holderman noted that a lot of good material is being developed that would serve this purpose. If CFSAC gets a yes from the HHS Secretary, it would be a matter of selecting from those materials.

While waiting for members to return to the room so that there would be a quorum for a vote, Dr. Lee noted that CFSAC approved a recommendation at its November 2011 meeting that CFSAC get feedback from the Secretary on what is done with its recommendations. The leadership team had a conference call with Dr. Koh in January 2012, and he committed to making sure that he gave feedback. In the meantime,

the higher-ups in HHS found it to be a potent recommendation. CFSAC staff worked with the *ex officios* to develop a document for the Secretary to use when responding to the committee. It includes lots of detail beyond "thank you for your recommendations." The document is now in clearance. Dr. Lee said she hopes to disseminate it to CFSAC members soon and hopes that it is a model for the future.

Dr. Lee then read Ms. Holderman's recommendation on education, which was seconded by Dr. Corbin.

The recommendation passed unanimously.

Dr. Lee said that CFSAC could address Dr. Dimitrakoff's biomarker white paper idea in the subcommittees. She noted that the paper could not list authors as CFSAC members without a lengthy clearance process, but that CFSAC could support the effort with conference calls.

Dr. Lee described the meeting as "very productive."

Ms. Holderman noted that the case definition issue is very important and timely and that CFSAC needs to move on it. She said the day's discussion on the subject produced the makings of a recommendation.

Dr. Lee: What I would like to see is some hard work in the subcommittees. That's my challenge to you guys. I challenge you to make this happen. We are here to work with you on that.

Ms. Holderman noted that the agenda did not include subcommittee reports on activities since the November 2011 meeting. Dr. Lee said that written reports could be posted on the CFSAC website along with other meeting materials.

Dr. Lee adjourned the meeting, thanking members for their work and support.

Adjournment

Public Comment

The following are brief highlights of public testimony delivered at the CFSAC meeting. [Please click here to see the texts of complete statements.]

Karen Lambert

- I have chronic fatigue immune dysfunction syndrome (CFS/CFIDS/ME) and NON-HIV AIDS, idiopathic CD lymphocytopenia. With these two diagnoses, I believe that makes me living proof that the AIDS-like CFIDS/ME is transmissible. I also believe I am living proof that CFIDS and NON-HIV AIDS are the same immune disorder.

- Why isn't CFIDS/ME a reportable disease overseen by our health department? Why are ME and CFS—the same exact disorder—categorized as two separate illnesses on a worldwide level? Doesn't anyone else but me very clearly see the catastrophic cover up going on?

- I want to know why CFIDS and AIDS are not looked at together as one illness if in fact it's believed that they are caused by a retrovirus.

Rev. Bernard F. Hillenbrand

- I speak for the hundreds of thousands of people whose loved ones suffer with CFS. They are as much tormented by this disease and doing as much suffering in their own way as if they actually had it. I have been in that category for 25 years. My daughter was doing beautifully in school. She had a 3.8 average and was an athlete. She suddenly fell very ill with CFS.

- We seem to have lost hope. My experience with in dealing with people who have CFS is that they have a feeling that it's never going to change. That it won't get solved.

- We conquered polio and it was a triumph. AIDS today is not the death sentence that it once was. Kimberly McCleary, as president of the CFIDS Association, has started what I call the new March of Dimes—a research program that is determined to make a difference. Yesterday the CFSAC chairman told the pediatric CFS patients that "just because you have CFS now doesn't mean you're going to have it tomorrow." I want personally to accept that as my own pledge and spend what time I have to do every single thing I can to bring hope and enthusiasm.

Ed Jalinske, PANDORA Director and Senior Policy Advisor (read by Tina Tidmore, PANDORA communications advisor)

- We are pleased to see that the Special Emphasis Panel for CFS is now named correctly and is only for ME/CFS. The improper name led to grants that should have been used for ME/CFS being used in research for other diseases. How soon will NIH refund the approximately $18.5 million to true ME/CFS research?

- We ask Dr. Belay to assist us in finding out why the CDC's National Center for Health Statistics has still not announced a decision on ICD-10-CM. We also ask that the CDC correct the mislabeling problem and double -standard on its CFS website page titled "Improving Health and Quality of Life."

- The new CME video on Medscape sponsored by the CDC is an improvement over what has come from the CDC in the past, but the discussion on "illness behavior" could give the impression that patients display this behavior because they want to remain on disability. What an awful and misleading message to give to physicians.

Samantha Hodge-Williams (via phone)

- I encourage the CDC to include a link to the physician's primer in lieu of the toolkit. The CDC toolkit should be removed until it has been updated.

- Do not shorten or simplify the primer. Although I don't have any medical training, I was able to understand the primer. Providers need at least this minimal information in order to diagnose and treat ME/CFS patients, especially the information about orthostatic intolerance and its treatments.

- I support CFSAC becoming the designated HHS experts on ME/CFS, so all agencies have to get the committee's approval before they post information to make sure it's accurate.

Matthew Fairman

- To state that ME/CFS is comparable to late-stage AIDS, congestive heart failure, and MS does not begin to convey the severity of this illness. The harsh, soul-crushing reality of an incurable disease that strait-jackets the bodies and minds of its victims is lost in translation.

- It is beyond travesty that ME/CFS receives such an outrageously small sum of taxpayer funds for research, while other illnesses of similar severity (and often smaller patient populations) receive hundreds of millions and even billions of dollars for research. When this illness is one day solved, it will be obvious that those we trusted as stewards of the public health were too busy, too inattentive, too locked into erroneous, outmoded preconceptions to realize how vastly they were failing to meet the trust we put in them.

- The most frustrating thing about living with this illness is knowing that with all this horrible suffering, the one thing that stands in our way is the people at the NIH, FDA, and CDC who, in 30 years, have never taken this illness seriously. How many more of these meetings do we have to listen to civil servants pass the buck year after year after year?

Joseph Landson

- The history of ME/CFS and its previous incarnations seems to be a story of the same concepts and models getting recycled over and over. It is important to have statistically significant results from large aggregate data sets, but at the end of the day, isn't it more important to ask the right questions? To frame the problem in the right way? Many researchers are not yet asking the right questions about ME/CFS.

- Maybe if we get a unifying hypothesis of ME/CFS that makes sense, we can all be swinging in the same jungle rather than so many different disciplines each describing the illness in its own untranslatable way.

- The fractured research vision may be contributing to the underestimation, underfunding, and continued disdain for ME/CFS and its patients.

Jennifer Spotila (via phone)

- Despite all the efforts you have made in making recommendations to the Secretary, there is very little action to report. In the last 20 months, only three of your recommendations have been marked with updated responses. Many of the recommendations marked as complete have not been accomplished as you intended.

- I don't believe that meeting, planning, and website content review are where you can add the most value to the policy and agency responses to ME/CFS.

- We always hear nice promises at these meetings. There is always the illusion that progress is being made, that things are beginning to change. But to me, the lack of progress on your recommendations and the lack of accountability at HHS for ignoring them is the true barometer of where we are. Don't mistake updates for real progress. Keep track. Keep asking.

Dr. Lee thanked all those who testified and who assisted those who could not speak by reading their testimony. "It is always very important that we keep ourselves real here in this committee and I appreciate your efforts," she said.