



CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE

Meeting

Wednesday, May 27, 2009
9:00 a.m. to 5:00 p.m.

Thursday, May 28, 2009
9:00 a.m. to 4:00 p.m.

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

Agenda Wednesday, May 27, 2009

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	<u>--Family Perspective</u>	pg 113	Lauren Allen Mrs. Peggy Allen <i>Utah</i>
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	<u>--CFS and FII/MBP</u>	pg 100	Dr. David Bell <i>Lyndonville, New York</i>
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CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE

Voting Members

Chair

James M. Oleske, MD, MPH, CIP Newark, NJ	Term: 01/03/06 to 01/03/10
Rebecca Artman Middleburg, FL	Term: 01/03/06 to 01/03/10
Lucinda Bateman, MD, PC Salt Lake City, UT	Term: 01/03/06 to 01/03/10
Ronald Glaser, PhD Columbus, OH	Term: 04/01/07 to 04/01/11
Arthur J. Hartz, MD, PhD Iowa City, IA	Term: 04/01/07 to 04/01/11
Kristine Healy, MPH, PA-C Chicago, IL	Term: 01/03/06 to 01/03/10
Leonard Jason, PhD Chicago, IL	Term: 04/01/07 to 04/01/11
Nancy Klimas, MD Miami, FL	Term: 04/01/07 to 04/01/11
Jason Newfield, Esq. Garden City, NJ	Term: 07/01/06 to 07/01/10
Morris Papernik, MD Glastonbury, CT	Term: 01/03/06 to 01/03/10
Christopher Snell, PhD Stockton, CA	Term: 04/01/07 to 04/01/11

Ex Officio Members

Centers for Disease Control and Prevention (CDC)

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

Ermias Belay, MD (*Alternate*)
Associate Director for Epidemiologic Science; Division of Viral and Rickettsial
Diseases; National Center for Zoonotic, Vector-borne, and Enteric Diseases

Food and Drug Administration (FDA)

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

Health Resources and Services Administration (HRSA)

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

National Institutes of Health (NIH)

Eleanor Hanna, PhD
Associate Director for Special Projects and Centers
Office of Research on Women's Health

Social Security Administration (SSA)

Laurence Desi, Sr., MD, MPH (*Primary*)
Medical Officer
Office of Medical Policy

James Julian, Esq. (*Alternate*)
Director
Office of Medical Policy

Executive Secretary (Designated Federal Official)

Wanda K. Jones, DrPH
Deputy Assistant Secretary for Health (Women's Health)
Director, Office on Women's Health

Wednesday, May 27, 2009

Call to Order/Opening Remarks

Dr. James Oleske

Dr. Oleske called the Chronic Fatigue Syndrome Advisory Committee (CFSAC) meeting to order, welcoming panel members and thanking them for their attendance, loyalty, and hard work over the last several years. He also welcomed visitors, guests, and presenters, noting that the most important part of each CFSAC meeting is hearing the challenges that chronic fatigue syndrome (CFS) patients face so that the committee can make recommendations that meet their needs.

Dr. Oleske noted that since the October 2008 CFSAC meeting, the nation has elected a new President and the committee has a new Department of Health and Human Services (HHS) Secretary to advise. "With any start, it's important for us to be diligent," said Dr. Oleske, "and at this meeting, take advantage of the opportunities that may avail themselves for funding and support for what we feel is a critically under-funded illness—CFS."

Roll Call, Housekeeping

Dr. Wanda Jones

Dr. Jones added her welcome to meeting attendees and conducted roll call using the roster of committee members as posted on the CFSAC website. A quorum of ten out of 11 voting members was present, with Dr. Papernik still en route to the meeting. Four out of five *ex officio* members were present, with Dr. Cavaille-Coll still en route.

Dr. Jones announced that the meeting was being web cast for the first time and credited the NIH web cast team and Total Audio Visual Systems for making necessary arrangements in less than one month. She then described the logistics of filming, noting that "there will probably be some bumps and some things that we'll be able to do better next time":

- One camera with zoom capability for tight shots was focused on CFSAC members. This camera also captured committee member and round table discussions and all audio visual aspects of presentations (PowerPoint slides, DVDs, public comments via telephone, etc.).
- One unattended fixed-focus camera filmed *ex officio* members.
- Both cameras were located behind presenters and did not capture their faces, although their audio visual materials were videotaped.
- Audience members were not videotaped due to privacy considerations.

- CFSAC will explore with the CFS community other ways to increase meeting accessibility.

Dr. Jason: On behalf of the committee as well as the many, many patients and folks from the community who have asked for this for years, we are just delighted and we want to thank you and your staff for making this possible.

Dr. Jones: We are committed to keeping this committee and chronic fatigue syndrome (CFS) visible within the department. We have heard some feedback, including some dissatisfaction with the fact that this committee is now being housed within the Office on Women's Health (OWH). My response to that is that the OWH has never discriminated against men. Women's health issues are men's issues; men's health issues are women's issues.

We see things through a gendered lens, and while CF does affect men and women differently, by housing this committee in the OWH, this is in no way meant to down pedal, downplay, or ignore the problems that CFS also poses to men. We are committed to a full understanding and appreciation of and respect for the sex and gender-based differences in health and in any number of disease conditions.

Dr. Jones then thanked the members of her staff who volunteered their time to support CFSAC, including those serving as building escorts in accordance with HHS security requirements:

- Capt. Marian Mehegan, a dentist by training who is based in the HHS Boston regional office, provided lead support via email to the CFSAC support team in Dr. Jones's office.
- Mahak Nayyar, a program analyst in the Office of Public Health and Science, made IT improvements in CFSAC's online visibility and linkage to other relevant information.
- Saba Gebrekristos, a temp in Dr. Jones's office, photocopied the extensive sets of background, presentations, public testimony, and other materials made available to committee members and the public.
- Linda Price, Dr. Jones's secretary, interacted with committee members and public commenters.
- Loretta Jones tended to a variety of meeting logistics, including room reservations.

Dr. Jones also noted upgrades to the CFSAC website:

- The CFSAC meeting web cast will be archived, captioned to be fully 508 compliant, and accessible via a link on the CFSAC website.
- The CFSAC main page will continue to include links to highlights and notices.
- The CFSAC main page has been enhanced to include links to direct information for patients, consumers, caregivers, and others interested in CF.

- Public testimony from the May 2009 meeting will be available on the CFSAC website along with committee recommendations and the meeting minutes.
- The CFSAC website has improved linkages to the sites for the CDC, OWH, NIH, and other HHS websites. Continuing improvements will be made to the accessibility of information across HHS and SSA.

Agency Updates

Note: Dr. Papernik arrived and took his seat prior to agency updates.

HRSA Update

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

Dr. Willis-Fillinger noted that since the October 2008 CFSAC meeting, HRSA got a new administrator—Mary Wakefield, PhD, RN. Dr. Wakefield has a distinguished history of support for workforce and healthcare quality, improvement, and access, particularly in rural communities, said Dr. Willis-Fillinger. Dr. Wakefield served on the committee that produced “Crossing the Quality Chasm,” a 2001 report compiled with the Institute of Medicine.

Dr. Willis-Fillinger reported that HRSA’s Area Health Education Centers (AHECs) have expressed “a fair amount of interest” in finding out more about CFS. She did not know the actual number of requests for training, but assured CFSAC members that she would report such statistics when they become available. Dr. Willis-Fillinger said that many of the AHECs have or are seeking NIH-related clinical translational research awards for connecting academia with communities to accelerate the translation of science into practice. About six AHECs have received awards and another six have applied.

Dr. Willis-Fillinger reported that HRSA has received American Recovery and Reinvestment Act (ARRA) funding that will go towards expanding access to healthcare at the community level. This includes funding for construction, expansion, and workforce development of HRSA-supported community programs. She explained that with a tight turnaround time, HRSA has been busy for the last several months ensuring that ARRA funds are spent in a transparent and effective way.

Dr. Willis-Fillinger closed by stating her support for CFSAC and her willingness to communicate its wishes to HRSA.

Committee Discussion

Dr. Jason: How much ARRA money is coming in? Is it possible that any of those new funds could be put towards the CFS research and practice community interacting with your office over the next two years?

Dr. Willis-Fillinger: Right now I can't give you the dollar amounts, but the funds are specifically focused on expansion of access to healthcare through construction or expansion of clinical services. HRSA is focused on healthcare in general and does not have a disease-specific focus except for HIV, where there are funds that have been specifically identified for HIV/AIDS care.

Decisions depend on each community and its focus on the ground. There may be, for example, an individual provider who has expertise in CFS who is practicing in one of the programs or centers that we fund. That's not something that we direct from our seats here in Washington. The funds are given to community-based organizations that direct the care based on community needs. I can't say that ARRA funds would be directed towards CFS unless there was a community focus.

Dr. Papernik: How do we get the communities to focus on a specific type of issue? For example, one of the letters that I received prior to this meeting discussed a patient who was having trouble finding a physician in the Atlanta area to treat CFS. To me that sounds like a community in need of a physician for that particular disease process. It is patient-specific in that there is a need for that type of access in that population.

Dr. Willis-Fillinger: That's a good question. Much of the funding that we support goes to community-based organizations. Those organizations do a needs assessment for their communities to determine staff support based on their priorities. Many are high-need communities for a lot of disorders, including cardiovascular disease and hypertension. I think that we run into the same situations that you run into in general. If there is a small community with CFS versus a larger community with other needs, they'll have to balance their focus. If you know of particular community health centers where you think it would be appropriate to have a CFS focus, that would be of interest. But when organizations do a needs assessment, they do a general assessment. It's not focused on any one particular disease.

Dr. Jason: Whom do we address that to? Is there a specific person in charge of doling out the needs of a particular community or is it based upon disease numbers?

Dr. Willis-Fillinger: Many times the communities look at numbers. The community board members as well as the clinical staff have a sense of what they are actually seeing regularly in their programs.

Let's do a hypothetical. If there was a situation where patients actually have CFS and people are concerned about it, then it's usually up to the individual providers and their own health professional development how to approach that particular situation. What we've been talking about here is really how providers address the issue of CFS when they see it. We have directed the clinicians to the CDC website and other websites to help them with their diagnostic skills. In the past we have sent letters to the community health centers talking about CFS and making sure that the health professionals there are aware of it. Then it becomes an individual provider's responsibility.

If you're talking about the ARRA funds in general, they are used to expand healthcare availability in general. They are not focused on any particular disease. Connecting the ARRA funding with the need for health professional education specifically targeting CFS is not something that we would traditionally do.

Dr. Klimas: If the needs assessment does not include CFS-specific questions, then of course you don't know what the need is. The incidence of CFS is very similar to that of breast cancer. Maybe the needs assessment needs to include these questions. I would say that if we offer it, they will come, because there is no other place to go. This is a very silent disease in which 85 percent of patients are undiagnosed. It's not going to be on your radar unless you put it there. I would ask that the needs assessment—however that process is done—include questions that would identify this need.

Dr. Snell: It's a catch 22 situation. If you can't get the illness diagnosed, then you can't really do a needs assessment.

Dr. Oleske: To me, the rapid dispensing of money in two years to stimulate the economy runs contrary to doing good research. It's frightening to me to think that a lot of money will go to people dusting off grants that never got funded—that researchers thought were never going to get funded—that are being resubmitted because of the rapidity with which stimulus money must be spent. That bothers me, because with any chronic disease, it's hard to do something in two years.

I think there needs to be some new thinking about that concept. Yes, we want to stimulate the economy and yes, one of the ways is to get money into research, but you want to get the money into research that will look at real problems that Americans have and improve their health so that they can take part in the life of the communities that they live in. I don't think that there's a disconnect there.

I don't know what the answer is. It seems to me, though, that NIH leadership needs to say to the Executive Branch that it isn't possible to spend money in two years for anything other than acute illnesses or already-established programs. When you have a disease like CFS, we won't be part of that, and that's frustrating to me.

Dr. Willis-Fillinger: The funding that we received is not funding for research. It's specifically funding for infrastructure to expand the number of access points for primary care. I can't address your question directly.

Dr. Jones: When we get to the NIH update, perhaps Dr. Hanna can address it. We asked all of the *ex-officios* to be prepared to discuss anything being done with ARRA funding.

Dr. Hanna: I can address that right now. During his Congressional testimony, [NIH Director] Dr. [Raynard] Kington was asked about whether he thought they should extend the two-year time period, so people in Congress are having these kinds of questions.

Dr. Jason: I think that as you heard from the committee members today as well as in past sessions, access to care is a critical issue not only from what patients tell us, but from our own clinical practices. Given the importance of your agency [HRSA], we're just going to continue to ask these questions. We hope to be able to think through with you how there might be ways of us impacting those needs assessments and figuring out ways that the research community and the practitioner community can interact in a more articulated way with your agency. There are potential collaborations and potential ways that we can work together.

Ms. Artman: What can patients do individually and as groups—if they do not have the funds to see a primary doctor and are going to AHEC facilities—to encourage the doctors they see to be aware and take advantage of the information that you've sent out?

Willis-Fillinger: I think that providers are very sensitive to their patients' needs. Many CFS patients are well informed—bring your literature, websites, and other information with you when you see your practitioner. It helps communicate with him or her in terms of what your needs are. It helps the practitioner put a face with CFS if he or she is not making the connection between a particular patient's concerns and CFS. Just having that information available is always helpful. As with any other provider, communicating with a provider at a community health center helps to elevate his or her awareness of the number of people who may be affected with those symptoms.

Ms. Healy: When a letter goes out such as those sent to AHECs advising them of resources at CDC and elsewhere, those efforts are helpful at the time they occur, but they are not sustained. Lots of state licensing boards require specific kinds of continuing medical education. Would community health centers consider requiring that every provider—every physician, nurse practitioner, physicians assistant, psychologist, etc.—have some sort of continuing education to ensure that they are able to recognize and treat patients with a preexisting diagnosis of CFS or those with the many symptoms and difficulties associated with this condition? I don't know whether there would be any consideration of such a requirement for community health centers that receive HRSA funding.

Dr. Willis-Fillinger: The approach to health professional development is something that is currently being discussed, so I'll certainly bring back your comment. The traditional approach is to require certification, licensure, and a certain number of CMEs [continuing medical education]. Traditionally healthcare institutions do not dictate what types of CME a provider should get. That's usually left to the discretion of the provider. But I will certainly take back your idea.

SSA Update

Dr. Laurence Desi, Medical Officer, Office of Medical Policy
Accompanying Document: *Programs Operations Manual Section DI 26510.015*

**Completing Item 16A and 16B (Primary and Secondary
Diagnosis, Body System Code and Impairment Code)
on the SSA-831**

I looked over the minutes from the October 2008 CFSAC meeting and I have nothing to add or expand upon from that. To my knowledge, SSA does not have any specific programs involving CFS that are receiving ARRA funding.

Committee Discussion

Dr. Klimas: As I recall, there were two major issues at the October 2008 CFSAC meeting. One was the speed with which disability cases are reviewed and awarded. I would have hoped that the stimulus money might have helped speed up case review. The other issue was regional differences between approvals and non-approvals. I think it's a question that's been asked many, many times in the many years that I've been on and off this committee, and I don't recall ever really getting a sense that we knew the answer to that. There's a sense among the disability attorneys whom I talk to that there are some locations where a patient would rather not have this disease and hope to get Social Security approval and locations that are better.

Dr. Desi: With regard to the rapidity with which claims are adjudicated, I'm not aware of funding specifically for CFS claims, but in terms of claims in general, the SSA Commissioner is increasing the number of administrative law judges and support staff so that when somebody gets to that part of the appeals process, hopefully those claims will be adjudicated more rapidly. We're also ramping up our use of health information technology for processing all claims with the anticipation that processing will be more efficient and rapid. With regard to the regional differences, unfortunately I can't provide you any insight into why that may or may not occur.

Dr. Klimas: I'm concerned about that answer because it seems like that's something that could be easily answered—the rate of cases coming to review and their approval rate by disease. If CFS is the disease in question, there should be approval rates accessible. This very serious concern should be addressed by your agency.

Dr. Desi: All I can tell you is that we have taken the step of adding a specific impairment code for CFS so we can track that particular claim. In other words, if someone claims that as a disorder and the claim is adjudicated based on that disorder, then that would be tracked. It gets somewhat complex in that patients who have CFS may be awarded disability based on chronic heart failure. You're more likely to see the coding for chronic heart failure than for CFS. I can forward your request to management as I did with the other requests from the last meeting.

Dr. Jason: I just wanted to second what Nancy said. It would be very helpful if perhaps between this meeting and the next one, or at the next meeting and on an ongoing basis, you could provide this committee with those statistics. To the extent that we have that data, we can ask more specific questions.

Some studies that have been done with different illnesses show that CFS and FM often get rated at the low end in terms of prestige. I'm wondering whether medical and other personnel who do some of these SSA ratings might have differential attitudes towards these illnesses. Has that ever been studied, or do you ever have internal studies to look at potential biases in the evaluation process?

Dr. Desi: We evaluate complaints that come in. Our primary source of medical evidence comes from the claimant's treating sources. If that information is insufficient for us to make a determination, we may request additional information or get a consultative examination to further evaluate that individual. It's a very clear policy at SSA. We have a ruling that addresses CFS. Other than that, I'm not quite sure that I can address what your concerns are.

Mr. Newfield: When was that impairment coding first implemented?

Dr. Desi: I believe it was last year, although I'm not certain.

Mr. Newfield: What timeframe do you think would be appropriate for us to be able to get that data so that we can evaluate it and potentially interface further with you on those issues? Are we a year into that? Is it not yet a year? I know that we've been talking about the issue of getting the data for a number of years. Prior to that, you said there wasn't proper coding. Now that we have the coding in place, the question is how can we secure that information and work with it?

Dr. Desi: That would go through our management information system. That would be a query that I would have to pass up to senior management to have them respond to that. I can't make that assessment.

Mr. Newfield: Following up on Nancy's point on regional potential biases, from my experience, even within a region there are judge-specific biases, so I'm not sure you can really attribute it to any region or location. All of the judges bring their life experiences to adjudicating these claims whether it's in the SSA context or others. I'm not sure there's any useful information that we'll get from that.

Dr. Klimas: But as a clinician who takes care of a lot of patients from many different regions, I can say that there is a perception—and it might be just a perception—that there are some places where you will never be approved; there are some regions where there are no judges who perceive this and no judges who follow the guidelines that the SSA put forth. I think that you could take a look at data by region and then you certainly could go judge by judge. Is there a judge who has never approved a CFS case despite cases being in front of him or her?

In terms of cases that have some co-morbid conditions that are influencing the severity of the illness—there are a lot of such cases—that kind of thing will statistically even itself out. It's not a perfect tracking system that we would be looking at, but to not take a

look at all because a system's not perfect, I think, is wrong. I would ask that you do put that query through so that you can bring the response to the next meeting.

Mr. Newfield: I want to further that and ask you, is it possible that we don't have to wait until the next meeting to get that information? Perhaps between CFSAC meetings our subcommittees could get that information so we can use it in terms of our agendas.

Dr. Desi: I'm wondering if the most expeditious way of answering these questions is for the committee members to formulate them as a list. Then it's much easier for me to take that list and send it up the proper management channels for a response.

Dr. Bateman: I was just referring to the minutes from the last CFSAC meeting. The very first thing that you said was that you'd formed an ad hoc work group to address the concerns of the CFS community and were reviewing the guidance you give adjudicators to make sure that the instructions are consistent with the current state of the art. I'm wondering if you could give us a specific report about this ad hoc work group, what the work group has learned, and what they're planning to do.

Dr. Desi: Unfortunately I can't give your more specific information other than to say that we will be looking at educational opportunities for adjudicators. With regard to specific regulatory guidance, that I can't comment on.

Dr. Oleske: Why you can't comment on it?

Dr. Desi: We're prohibited by statute from commenting on any pending, proposed, or considered rules or regulations.

Dr. Oleske: I don't know if you have a sense of it, but the committee is really unsatisfied with the answers that you're giving us. We were told at two previous meetings that SSA was going to make sure that there was a sense of fairness throughout the country in the adjudication of cases, that there weren't regional differences or biases, and that people with CFS had their needs assessed on the reports that the judges received rather than feelings that CFS is or is not an illness. We're past that, and yet what we're hearing at this meeting in 2009—after two years of focusing our concerns on patients with CFS being treated fairly by SSA—is very frustrating, I'll have to say.

I don't know what position you're in and how you were told what to say to us, but I'll have to say, we haven't heard anything new. There doesn't seem to be any movement on issues that are very important to the patients we either take care of or represent on this committee. I would hope that before the next meeting, we can be communicated with about this idea of regional fairness and appropriate adjudication of cases. That's critical if patients who are sick can't even get disability. I haven't heard that there has been a change. Give us answers, then.

Dr. Desi: The only answer that I can give is to tell you what official SSA policy is, and that's reflected in our CFS ruling. We recognize that CFS can be a medically determinable impairment provided there is proper documentation. That adjudicatory policy does not apply only to the states. SSA adjudication is set up as a Federal/state joint venture in which the states do the initial adjudication through the state Disability Determination Service (DDS). The CFS policy is the same whether the adjudication is done on the state level or anywhere up the appeals process within SSA. Those same rules apply to the administrative law judges (ALJs) as well. The ALJs operate independently of the DDS decision. In other words, each decision is a *de novo* decision.

Why there are regional differences and how judges look at that, I don't know. As I said, we base a lot of what we do—our determinations—on the medical evidence provided by the claimant, which comes from the treating source. I am sure that there are differences in the medical community, and depending on what medical information comes in, it may make a difference in how the case becomes adjudicated. Without looking at a specific case, it's hard to give you a specific answer.

With regard to the specific queries that you made, all that I can do is take that information and pass it up through management. I don't personally have access to that information. That's why I thought that perhaps the best way would be for the committee to formulate a specific list of questions that can then be sent forward.

Dr. Oleske: Two years ago, there was an issue about this, and an internal SSA working group was going to look into it. Dr. Bateman read it to you. Sure, we can generate a list, but two years from now it will be disappointing if we come back and the working group hasn't met.

Dr. Desi: I understand your frustration. Unfortunately, I'm not at management level; I'm at staff level, so all that I can do is pass that up to management level.

Dr. Jason: We have indicated at least a couple of questions, with regional variation and the adjudication process being central. Perhaps if we could again make that request, which three people have made today and others have made in the past, we can see if we can get some movement. There are lots of other questions we have that we would like to follow up on—in particular, as Jason indicated, individual variation, which I think might be even more insightful. The reality is, we have to start somewhere, and so if we could make this request to you formally and see if we can at least get something back from people above your office who can get this information to us, then we can start this dialog process and have further questions as well.

Ms. Artman: I think that there are a couple of very specific things that we would like to ask from your office. This can be an official suggestion, not a recommendation. To date, how many people with CFS have applied for Social Security disability? About four and a half years ago, we were told that between 700 and 800 people were approved and on Social Security disability for CFS, which given the number of people with this

illness and how disabling it is, is shocking. I'd like to find out how many people have applied, how many people have been approved out of that number, and then the numbers that Nancy is talking about—is there a regional bias? Those three specific things would be very beneficial for this committee and for your administration to know.

Dr. Desi: There's a difference between regional bias and regional variation. There may be regional variation without regional bias. I think that it's important not to confuse the two terms.

Dr. Papernik: Are adjudication decisions in the public domain? Can you look up anywhere in the government database to find out how many people with CFS have been denied or adjudicated favorably for disability?

Dr. Desi: I'm not sure. My sense is that it probably is not, mainly because the database itself has personally identifiable information with the adjudication. For someone to use those records, they would have to be sanitized prior to use. That's not just for people outside the government. If we have research done by another government agency such as NIH, those records need to be sanitized before they move outside of SSA.

Dr. Snell: Last meeting there was a discussion about SSA starting to do coding for illnesses such as fibromyalgia (FM), Lyme disease, and CFS. We made a formal request to see if we could get a list of those codes so that we could actually see some of the illnesses that share some symptoms with CFS and ask questions other than those directly related to CFS. Is it possible to get those codes before the next meeting? Give us the whole code list, and then we'll decide what we think might be under the rubric of CFS.

Dr. Desi: As I said, I think that it would be appropriate for the committee to make a formal request. I think that it would get a better response. I don't know if anything from this committee has gone directly to the Commissioner of Social Security. I've taken information from our previous discussions and sent it up through my chain of command. That's the limit to what I can do.

Dr. Snell: It's important that we know that if we make a formal request verbally in this meeting, is it a formal request or do we actually need to put it in writing?

Dr. Desi: I would put it in writing.

Dr. Oleske: I think that we have that responsibility. We've done that already, but I think that we need to do that again on this particular issue.

Mr. Newfield: You're saying that we should direct our attention directly to the Commissioner with regard to these queries?

Dr. Desi: I'm the Social Security representative on this committee. If you have queries, if you send them to me, I will forward them up my chain of command. I'm not going to say that you can't directly query the Commissioner himself.

Mr. Newfield: We just want to know what's going to be most effective. We don't want to step on toes; we just want to get answers. What's going to be the most effective mechanism to accomplish that?

Dr. Desi: From my perspective, I would have to say to send me a formal written request and I will send it up my chain. If that doesn't get you a satisfactory response, then you may have no other recourse than to query the Commissioner himself.

NIH Update

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

Accompanying Documents: *Second Annual Meeting of Neuroimmune Mechanisms and Chronic Fatigue Syndrome Principal Investigators; Final Opportunity to Attend a 2009 NIH Regional Seminar on Program Funding & Grants Administration, Notice Number NOT-OD-09-102; Trans-NIH Collaboration on Chronic Fatigue Syndrome*

The new thing that we have planned this year is going to be the Second Annual Meeting of Neuroimmune Mechanisms and Chronic Fatigue Syndrome Principal Investigators, "From Infection to Neurometabolism." We're sponsoring that in collaboration with the Banbury Center, which is where the meeting will be held. Suzanne Vernon from [the] CFIDS [Association of America] participated in the planning.

Dr. Hanna also distributed:

- An announcement of an NIH regional seminar on program funding and grants administration being held in Las Vegas on June 25-29, 2009.
- The chronic fatigue section of ORWH's biannual report to Congress for fiscal years 2007/2008. The CFS information was placed in the last NIH Director's report and Dr. Hanna anticipates that the 2007/2008 section will be as well.

Dr. Hanna: If you go back to Dr. Kington's testimony before Senate hearings [Labor, Health and Human Services, Education, and Related Agencies Appropriations Subcommittee] last week when he presented the NIH stimulus funding, [Subcommittee Chairman] Sen. [Tom] Harkin [Iowa] asked him what he thought about the timing, which was very much in keeping with what was said this morning. I think there's some interest in working with that.

Coming back to the community programs and the questions you asked about participatory research, that's one of the big signatures of the stimulus funding. I sit on

the NIH committee that's designing the program announcement for those new participatory centers. Perhaps there's a way that I can take a look at how they're going to do the needs assessments. I'll keep an eye open on that.

Committee Discussion

Dr. Oleske: When I went through the stimulus grants that were due less than a month ago, there were a lot of categories that I thought could be taken advantage of by CFS investigators. For example, there are monies being put into the office that is in charge of palliative care. I called them up and talked to them about what they do, and it's not just hospice, but includes areas such as pain management. It's important to recognize that while there should be an office that's coordinating grants to address issues of CFS/encephalomyalgia, if you go down the various categories, a lot of them are research that addresses issues that relieve similar symptoms and signs.

Dr. Hanna: It's something that I brought up at the grantsmanship workshop that I did by phone at the IACFS (International Association of Centers for Federal Studies) meeting. One of the things I wanted to say is that it's very important that all currently funded CFS investigators discuss with their project officers how they can develop supplements to their currently funded grants to take advantage of the ARRA goals—as long as it shows that it's a project that's going to expand current science.

The other thing that I tried to emphasize to researchers is to not be discouraged if ORWH is not listed in a challenge grant opportunity. The offices within the Office of the Director were not allowed to develop their own challenges or programs. We have petitioned to have funds and permission to do this. I wrote up something for CF specifically requesting funding for this network of researchers in order to really advance things. We haven't heard back on that, but we haven't given up on it. Meanwhile, every one of the challenge areas, I think, is ripe for applications for our CFS researchers. I think that there are people applying for GO grants [Research and Research Infrastructure "Grand Opportunities"] and challenge grants. I think we will see a lot of new funding coming in for that.

Dr. Jason: I have several questions. First, the CFS Special Emphasis Panel had an interim appointment for the Scientific Review Officer/Administrator for about the last year. I know that's within the Center for Scientific Review (CSR), but I wondered if you have any information about whether there's been an appointment.

Second, at one point in the past you had mentioned that there was some talk about potentially a new RFA (request for applications) specifically in this area to come out of a workshop. I was wondering if you could comment on whether there have been any further plans on that.

The last question—over the last year, has there been an up tick, a stabilization, or a decrease of grants that have been funded in this area at NIH?

Dr. Hanna: First of all, in terms of grant funding, I think things have remained stable. Secondly, in terms of CSR, I can't comment there, but you do remind me that I did want to thank some people in the audience including Terry Hoffeld, who is the former CSR chair of the panel and has helped enormously in our trans-NIH committee, and Sandy Solomon, who is visiting from Arizona. She was tremendously helpful to us on the website. The RFA was going to come from the investigators' workshop. And that's what I did apply for the funding for under ARRA. That's what it was going to be about—to set up a network of investigators.

Dr. Klimas: Speaking of networks, there was some effort to develop clinical trials networks coming out of the Reno meeting. There was a lot of discussion and the clinical trials networks concept was reframed at the Reno meetings. There is a desire to go forward looking for funding from different pots. I know there was a clarification of the current program announcement that that's not an appropriate place to house a clinical trials network.

Dr. Hanna: Yes, the NIAID (National Institute of Allergy and Infectious Diseases) announcement. I wanted to address that because I know that you were upset about it. I think that it does not mean that NIAID is not willing to fund CFS anymore. It means that they're going to be getting so many applications for clinical trials with the comparative effectiveness research and so on that they would like to centralize all of those applications in their own centers. They're inviting you to apply directly to NIAID for clinical trials. That's not something I would worry about in terms of CFS. If you want NIAID funding, you should put it there. Talk to your NIAID contact and ask them what they think. If you put it on the PA program, you're likely to get more institutes and funding.

Dr. Oleske: I think there are opportunities. I can say that they're freeing up monies by really drastically reducing the domestic agenda for HIV. I think that there is some bias against clinical trials because they feel they're expensive and use resources, but in fact, when I first joined this committee that was our very first recommendation—that a clinical trials center be created. I was very supportive of that because it worked well for AIDS. I would take the recommendation and go with NIAID if that's what we're hearing is recommended. There should be money in that pot.

Dr. Klimas: I will clarify my statement, because this is a webinar and people didn't explain why this is important. It's fairly straightforward through the program announcement to get funding for Phase 1 and Phase 2—the first two steps towards approval of monies to do clinical trials—because the research is usually within a single site. But when you move to Phase 3, you need a large number of subjects. The method would be quite wrong to do it within a single site. We need to network and we need to develop across regions and across multiple sites to be able to say with assurance that findings are correct, accurate, and predict what will happen when the drugs are released. Within the FDA, there's usually the requirement for two Phase 3 clinical trials to be completed before a drug is approved.

We are at the stage of CF research where there are a multitude of Phase 1 and 2 studies moving towards Phase 3, but we are locked because we can't move to Phase 3. We don't have a clinical trials network. We don't have a real mechanism to do that. For instance, you saw in the last few years three drugs approved for FM and a huge national public awareness campaign funded by the pharmaceutical companies that will profit. It was a huge boon to the FM patients to have some drugs and also to have knowledgeable physicians who understand that there are some therapies out there. Granted, it's not the best way to practice medicine to be driven by the pharmaceutical industry, but nonetheless, it served a very positive purpose.

CFS doesn't have a label on a drug yet. We have no industry support for public and physician awareness campaigns, so we're having to do it all ourselves, and that's part of the reason that this advisory panel is so very important. The question of clinical trials networks and how we plan to develop an infrastructure of centers that are capable of doing Phase 3 work is critical to the next big step towards effective treatment of CFS. I applaud the NIH for trying to help us move in that direction.

Dr. Oleske: I think the AIDS model showed success when you do have a large enough group to do the power analysis on studies. As a center that did pediatric AIDS, it was very clear that we could prove that we could prevent HIV, but we had to have multiple centers to have the numbers. And what did we do? Within three years we basically lowered the transmission from mother to child from 30 percent down to one percent or less. For CFS, it's not a bad model. It works. That's great that there may be a mechanism to do that. I think it should be applauded that this group stimulates that. I think that is really the step we need to take.

Dr. Jason: Over the years, this group has made a number of recommendations for the establishment of clinical trial centers for both research and patient care. It's fantastic that Wanda now has the recommendations on the website so we can look at them and see what they say. They are really consistent. It goes back to David Bell about four years ago with the ten recommendations that he made. It's also something that our committee has made again and again.

The stimulus money totals over \$10 billion, which is really incredible and is probably a one-time event for the scientific community to have access to these types of resources. Is there any way for your office or other offices within NIH to seize upon this opportunity to go beyond the \$4 million a year that is being focused on CFS research and fund clinical care networks, as we're suggesting?

Dr. Hanna: You need to keep in mind that the priority for NIH is research and not clinical care. Naturally how research informs clinical care is relevant. I can prepare some dollar figures for the stimulus money, which has pretty much been allocated. There are ways in which these things could be started out. For example, the thing that Nancy's talking about could have been applied for in one of the GO grants because that provides an infrastructure for expanding science.

There's no reason why—as I've said before—if you want to have centers that are going to provide education you couldn't apply for one of the ORWH BIRCIWH (Building Interdisciplinary Research Careers in Women's Health) grants. We will have a new offering coming up this year. I hope you look for that because it gives you an optimum way to train new people in research and clinical care.

Let me give you a rundown of the allocation of stimulus money for NIH:

- **\$1.3 billion for the National Center for Research Resources**, with \$1 billion for extramural construction and renovation and \$300 million for shared instrumentation and other large capital research equipment.
- **\$8.2 billion given directly to the NIH Director's Office**, with \$7.4 billion to the Institutes and Centers and the Common Fund. You'll see that money in specific institute grants that come up. I have Web links for you [in the written presentation] that will give you all of this. \$800 million will fund specific challenges and priorities. This includes the community participatory item that I was talking about. We're trying to get some of that money for the networks.
- **\$400 million from the Agency for Health Care Research Quality** to support comparative effectiveness research. AHRQ prefers to stick with its specialty and let NIH take care of the clinical trials. That research is going to be very important in changing healthcare delivery and reimbursement.
- **\$500 million for funding high priority repairs, improvements, and construction** on the NIH campus.

Keep in mind when you're applying for grants funded by ARRA that the goal is to stimulate the economy and create and preserve jobs as well as advance biomedical research. You have to keep all of the three in your comments.

Dr. Oleske: I would like to remind everyone, by the way, that I think we really should talk in millions of dollars because I don't think that people understand a billion dollars. So \$7.4 billion is \$7,400 million dollars. That is a lot of money and it makes the lack of support for specific diseases somewhat embarrassing. I think that CFS has fallen and I want to read something for the record. This is from August 2005, my first meeting here:

Recommendation #1: We urge that the HHS direct the NIH to establish five centers of excellence within the United States that would effectively utilize state of the art knowledge concerning the diagnosis, clinical management, treatment, and clinical research of persons with chronic fatigue syndrome. These centers should be modeled after existing centers of excellence with funding in the range of \$1.5 million per site for five years.

We were asking for \$5-6 million. Remember, one billion is a thousand million. I think that we should really thank Dr. Hanna this presentation and let's really take advantage of Recommendation #1 from 2005.

Dr. Jason: I'd be interested in getting your perspective on how we should take advantage of that recommendation.

Dr. Oleske: We are not a clinical trial group. There are some of us who don't participate and some who do. I think that the message that we send out in our recommendations are public knowledge. I would hope that people would now seriously think about getting a group together like we did with AIDS. We were overwhelmed, we didn't know what we were doing, and we knew we needed clinical trials. We kept applying. My first three grants for AIDS were turned down. You've got to make that first one. Given the stimulus package and all that's going on, we should encourage the groups that can do it to pull together a clinical trials network. That's the only way we're really going to help our patients.

Ms. Artman: When I was not on this committee and had gone to the Hill with that recommendation from Dr. Bell in hand, I was basically told by my senator's aide that the amount we were asking for was ridiculously low and that no centers of excellence could open for the amount of money that they were looking at. If we're going to reintroduce this recommendation, those of you who work in this field and know how much something costs should realistically figure out how much it's going to cost and attach that dollar figure to the recommendation. That's a serious issue, because it's not just this committee making a recommendation. People work with the recommendations that we put out there, so they need to be as dollar-accurate as possible.

Dr. Oleske: I think that number has changed drastically and I don't think this committee determines that. A group of investigators needs to get the money numbers together. That recommendation from 2005 is supported in spirit, but the numbers obviously need to be grossly changed.

Dr. Jones: Let me note for the record that when we did the roll call this morning, Dr. Papernik was not present. He did join us about 10 minutes or so into the meeting, so we welcome him amongst us. We're in the process of doing updates from the *ex officio* agencies and we do need to turn to CDC, but Dr. Marc Cavaille-Coll from FDA has joined us, so if you can give us a brief FDA update, then we will move on to the agenda.

FDA Update

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

It's very difficult for the FDA to make any updates unless new activities have taken place. The only things we are able to comment on are products that have been approved. Right now I must tell you that the new procedure that we have is that products that are not approved or provable will receive a complete response answer to the company. If we're dealing with products that are made by publicly traded companies, the publicly traded companies should make available to their shareholders

and to the public the information that the FDA has provided to them. But unless we approve a product, it's not possible for us to make a comment.

If and when we do approve a product, our reviews are made available on the Internet. They are redacted for issues that have to do with proprietary chemistry, manufacturing, and other issues. At this moment, there's nothing much we can say.

As I've said many times before, one of the complexities of developing new drugs for CFS is that we don't have any *in vitro* or any animal models that would allow us to select the products that would be potentially effective for this condition. In every other condition like hypertension, epilepsy—I'm just giving examples—immuno suppression for organ transplantation, there are models that do allow companies to select products that would be sufficiently effective or that would be worthwhile to be evaluated for those conditions. I think that CFS really challenges us because we don't have any type of model that allows us to select amongst thousands of molecules that would have potential. There's not much else I can say at this point.

Dr. Klimas: At the recent ICAFS meeting in Reno there was an effort to develop a clinical trials network. Earlier I was speaking with the NIH about how we would develop the infrastructure for such a thing. In your experience with other disease, how does the FDA interface with clinical trials networks so that we have the appropriate outcomes and the appropriate design that would lead to FDA approval at the end of all that work?

Dr. Cavaille-Coll: All I can tell is about my history working with products for AIDS. I was part of a study group for AIDS. I handled the lymph node and the blood of the first patient for which the virus was isolated. My experience at the FDA was with the AIDS clinical trial group. At that point, once we had identified the agent that was responsible for disease, we had a method to find agents that would be effective. I don't think that we're there yet with CFS.

Dr. Klimas: I'll ask my question a little more specifically. I had the privilege of coming to the FDA some years back in the design of a Phase 2 study with a company. I was just blown away by how wonderful the FDA was in reviewing and giving very appropriate, good, critical review of the design. A team of people reviewed the proposal in great detail, met with the researchers, gave them feedback, and really walked them through not just the FDA process for drug approval but also the FDA's sense of the outcome variables. Given what we have today—these measures are what we have to choose from, this is the illness as we know it—I think we would come as a clinical trials network and develop the best protocols we know how to develop. What I was hoping for was the same kind of interface with FDA as this drug company got. There's some way to do this.

Dr. Oleske: In the clinical trial network for AIDS, the FDA has been actively involved from the beginning of drug development for the treatment of AIDS and dosing. That's why you want to have a bonafide clinical trial network that's funded. I can tell you that the FDA has been wonderfully cooperative and there has been a very positive

relationship with the clinical trial network for AIDS. I think if we set up a clinical trials network for CFS, the FDA will come onboard. I think what I'm hearing is that the FDA is not in the position to establish a clinical trials network.

Dr. Cavaille-Coll: Establishing a clinical trial network is not the role of the FDA. I think what people do need to know is that for at least three years now, the therapeutic biologics have been integrated into the different drug areas in the Center of Drug Evaluation and Research, and we are working with that.

Dr. Jason: In the 1800's in Great Britain, a person named Snow did a very interesting epidemiological study where he found that people who drank close to a polluted source of water got sick with cholera even though the pathogen wasn't known at the time. By cutting down those water pipes or restricting access to them, officials were able to reduce morbidity and disease. Sometimes in our struggle to understand illness, not understanding the pathogens doesn't mean that we can't take important public health measures to help individuals who have disease illness.

Dr. Oleske: Actually, that's a very good point. We don't have to have the etiological agent. In fact, when we set up the AIDS clinical trials network, I don't think we had the agent yet. Those first networks were set up when we only had immunological markers.

CDC Update

Dr. Michael Miller, Associate Director for Science, *National Center for Zoonotic, Vector-borne, and Enteric Diseases (NCZVED)*

Accompanying Document: *CDC CFS Public Health Research Program 5-Year Strategic Plan*

We welcome our web cast participants and thank Wanda for the miracle of pulling this together in such a short time so that we can provide the CDC update to you. We had been scheduled for a two-hour portion of the agenda today to include both presentation and discussion. Hopefully we can still squeeze a lot of that in. You do not have the following items in your notebooks:

- The CDC did respond to the CFIDS comments at the last CFSAC meeting and we did present that to the committee for the record. We have no plans for any further discussion of that today.
- A new CDC Director has just been named. Dr. Thomas Frieden from New York will be joining CDC full time on June 1. He is an infectious disease-trained physician and should be a great asset to us.
- We had a recent public meeting concerning our five-year strategic plan that was held at the CDC and included a number of participants by phone. We felt that it was a very successful meeting. Remember, this is a process and the plan is still in development. The goal of that public meeting was to receive constructive

comments on how CDC could develop its five-year plan, and those comments helped shape the next iteration that we are presenting to you today.

Today's agenda will have two speakers who will combine four topics. CDC staff members accompanying me are:

- Sarah Wiley, Associate Director for Policy, NCZVED
- Stephan Monroe, PhD, Director, Division of Viral and Rickettsial Diseases, NCZVED
- William C. Reeves, MD, MSc, Chief, Chronic Viral Diseases Branch, Division of Viral and Rickettsial Diseases

The draft of the five-year strategic plan is the second document in tab #3 of your folder. This continued to be revised until Monday of this week and it will be further revised as a result of today's meeting. The strategic plan will be posted on the CDC website. The public and CFSAC certainly will be able to provide further comments at the CDC chronic fatigue website and at the HHS chronic fatigue website mailbox after you have an opportunity to study this. We would welcome your comments on how to constructively move forward with a strong research agenda.

Dr. Monroe will present an update on health marketing and the peer review that we had recently, then Dr. Reeves will present the research agenda with a research program update as well as the five-year strategic plan update.

Dr. Monroe

Accompanying Document: *CDC Program Update for the CFS Advisory Committee*

In the interest of getting us back on time, I'm going to try to go through my part of the presentation relatively quickly. The meat of the presentation on the strategic plan will be presented by Dr. Reeves. I'm going to give a brief update on activities that are coordinated through the National Center for Health Marketing and then talk about the process for the peer review that we conducted back in November. Dr. Reeves will present in detail the recommendations that came out of that peer review panel, the actions that have been taken to date, and the development of the strategic plan.

Public Awareness Campaign

Funding for the public awareness campaign does not come directly from the CFS appropriation. The money is set aside from other funds out of the Office of the Director. The last obligation under this activity was in fiscal year (FY) 2007, but public awareness activities continued through FY 2008 and 2009 with the expectation that they will be concluded in December 2009.

Summary of activities in 2008:

- TV public service announcements (PSAs) aired 2,570 times for a total of 45 million viewer impressions.
- Radio PSAs had projected plays totaling 16,530 on 256 stations for a total of 90.4 million audience impressions.
- The total value for free commercial airtime was \$1.3 million.
- The traveling photo exhibit, “The Faces of Chronic Fatigue,” was displayed in ten cities to an estimated 923,116 consumers. Media outreach using the exhibit as a news hook resulted in 172 print, broadcast, and online stories.
- CDC distributed 7,695 print copies of the brochure *Understanding Chronic Fatigue Syndrome: A Guide for Patients*. An additional 16,459 brochures were downloaded from CDC and CFIDS Association websites.
- CDC distributed 2,832 print copies of the *CFS Toolkit for Health Care Professionals*; an additional 53,818 fact sheets from the toolkit were downloaded.
- CDC distributed 2,300 print copies of the brochure for medical professionals, *Recognition and Management of Chronic Fatigue Syndrome*. An additional 9,943 copies were downloaded.
- Earned media (free outreach) resulted in more than 400 print, broadcast, and online stories that totaled millions in audience exposure.

Campaign activities planned through 2009:

- Photo exhibit in approximately seven public venues with earned media coverage.
- Tracking of TV and radio PSAs.
- A 60 second video on CFS disseminated via TV, online video hosting sites, and direct viral marketing.
- Distribution of collateral materials primarily through website downloads.
- Proposed working relationship with U.S.C. Hollywood, Health & Society staff to make sure that CFS is depicted accurately on TV and in film.

CFS Research Program External Peer Review Summary

Panel Member Selection

CFSAC made the original recommendation to have the peer review group and nominated potential reviewers at the May 2008 meeting. CDC also received input from its internal Coordinating Center for Infectious Diseases (CCID) Board of Scientific Counselors, external groups, and the research program itself. The five reviewers selected were:

Michael Boulton, CCID board member
 Anthony Komaroff, former CFSAC member
 Gudrun Lange, Veterans Administration
 James Oleske, CFSAC chair, who was unable to attend the review
 Peter White, London Queen Mary School of Medicine

Panel Review Process

Background materials: The research program prepared an extensive collection of summaries of programs, senior staff CVs (*curricula vitae*), and selected publications compiled into a virtual notebook that was sent to the reviewers in advance of the meeting on a USB thumb drive. They were presented a hard copy of the materials at the review.

Peer review format: The review was conducted over 2 ½ days and included:

- Slide presentations with plenty of time for Q&A. We didn't want to put people in a dark room, show them slides for two days, and say, "Thanks for your time."
- Poster presentations that allowed reviewers to interact more directly with some of the junior level staff, who were given an opportunity to showcase current work.
- Tours of the existing laboratory facilities. One of the CDC construction projects currently underway is a new laboratory—Building #23— which is expected to be finished mid-summer 2010. The CFS program is scheduled to move into that new laboratory in the fall of 2010.
- Interviews conducted by peer review members with senior and junior level staff both individually and in groups.
- Exit interviews with division- and national center-level staff.

It is a credit to the panel members that they prepared a draft report during the review, refined that report over the next week or so by email, and had the final version to us within two weeks. We were able to get that posted to our website within two weeks of the conclusion of the review, which was fairly remarkable.

Summary of Recommendations:

- Continue to support the CFS program so that the program can continue to do successful work.
- Develop a five-year strategic plan.
- Establish closer relationships with traditional public health (PH) agencies.
- Consider using existing database resources to further the understanding of CFS.
- Develop clinical guidelines.
- Consider studies that test causality.

Program actions:

- Develop five-year strategic plan—preliminary draft completed (next presentation).
- Form closer relationships with traditional PH agencies:
 - CFS program now has a fellow from the Council of State and Territorial Epidemiologists (CSTE).
 - CFS program members participated in the CSTE meeting in June.
 - CFS program has successfully recruited an Epidemic Intelligence Service (EIS) officer ("disease detective") at the annual EIS meeting. That person will be coming on board July 1 to begin a one-month training program that

is standard for all EIS officers, then be embedded in the CFS program beginning in August for the next 23 months. One assignment will be working more directly with state and local public health officials.

- Other recommendations incorporated into the five-year strategic plan.

Committee Discussion

Dr. Oleske: The EIS program is really a very strong program and having an officer experienced in CFS is a major step.

Dr. Monroe: Recruitment is a very competitive process. The EIS class numbers about 70 positions to be filled by physicians, veterinarians, research nurses, and epidemiologists each year. I envision it more like a fraternity rush where you go through a process of interviewing people during the week of the annual meeting. There are twice as many openings as there are people available to fill them. It involves convincing someone that this is important enough that they should commit two years of their training to working on this issue. We were successful in doing that.

Dr. Jason: With regard to the public awareness campaign, it's interesting when you talked about the need to influence the people who are producing some of the news. Dean Edell is probably the most popular physician on a radio program with probably the largest audience in the United States. In his broadcasts over the years, he has basically said that CFS is a hysterical illness. So you have a major physician who is constantly putting out that message and influencing people. He's probably not the only example of that. There is clearly a lot of work that needs to be done.

What do you think about people who do that type of work and who have a tremendous amount of credibility? What does it mean for the awareness campaign, with the funding ending in December? Are there any plans for a continuation of that feature?

Dr. Monroe: The Hollywood Health & Society group focuses primarily on TV and movies—fictional programming rather than nonfiction providers directly disseminating information. It's always a problem for CDC in almost everything we do—this debunking of people who come out with opinions that are contrary to prevailing medical evidence. How much effort needs to be put into that and how should we address that? We end up in a position of having to prove a negative. Somebody says something and then we have to prove that what they're saying is wrong. It's difficult.

What we've learned is that rote repetition of facts often doesn't work. Once an opinion has been stated, particularly if there's an emotional appeal to it, it's difficult for us to come back as a science-driven agency saying, "These are the facts. These are the facts." We're aware of what you're talking about, but it's hard for us to spend time debunking the messages of each individual.

In terms of the public awareness campaign, as Dr. Reeves will show, it looks like a lot of gains have been made. I know that there seems to be a discrepancy between what

we're measuring and what people are hearing in the field. I'm not entirely sure how to address that because we're going on what we've been able to measure. We will continue to do outreach through the channels that we have, but the specific funding for the traveling exhibit and other outreach is going to end with the calendar year.

Dr. Klimas: The peer review recommended development of clinical guidelines. I remind you that the IACFS/ME also has a clinical guidelines committee that is busily working on a couple of guidelines. I would hope that we would work together and not produce two different sets of clinical guidelines that confuse everyone even more.

Dr. Monroe: I certainly don't claim to be an expert on communication, but one of the things that I've learned from my little bit of training on risk communication is that you need to have consistency in messaging. Discrepancies in messaging are what really confuse people. I agree that we need to be coordinated.

Dr. Reeves

Accompanying Document: *CFS Research Program Draft Strategic Plan*

This was particularly hard to put together because it's a complex topic. I will give you much of the information that we gave to the peer review group over two days because you haven't heard this information in a cohesive manner.

1. I will explain the current program that we have on CFS.
2. I will discuss the logic model and why it is important. We use it to help guide strategy and evaluate our effectiveness.
3. I'm going to go through the current draft strategic plan and put it into the context of not only the peer review but also of the stakeholders meetings, comments that we've gotten from collaborators, and recommendations that this committee has made. The draft plan has been developed trying to take all of those into consideration.
4. I will discuss milestones, which will serve as a brief agency update of the research program. I would also be pleased to meet with the subcommittees.

1. Current CFS Program

CFS program objective – devise control and prevention strategies for CFS. The research is all intended to control and prevent CFS and improve the quality of life for those people who suffer it. We are not NIH, but CDC and NIH are very complementary agencies. I think that is important to keep in mind.

Control strategy – We have the population of the world, and some of those people have CFS. There is undoubtedly more than one sub-type of CFS. To control the disease, we need to get patients to interventions. People have to be evaluated and managed. That evaluation and management must take into account the multiple sub-types of CFS. Just getting at that is not trivial.

We can do all the things in the research program that we want to do, but if we don't actually make a difference, it's irrelevant. What we are very interested in at the most simplistic level is to decrease:

- The burden that CFS imposes on the population.
- The duration and severity of the illness in people who have it.
- The impairment.
- The economic impact.

People have to have access to healthcare before they can be treated and so the model and the strategy has to consider access to healthcare. If there are barriers to that, what are they? How do we address them?

People have to use the healthcare. You can have access, but if it isn't important enough to you, you don't understand that you can use it, or third parties don't pay for it, those are important barriers.

People have to receive appropriate care.

I think that what I've gone through to this point is of particular interest to all three of the subcommittees. and that's why one might consider all three subcommittee discussing these things instead of one. Each has its own very specific interests.

CFS is a Complex Illness

- Represents alterations in complex homeostatic systems.
- Not the result of a single mutation or single environmental factor.
- Arises from a combined action of many genes, environmental factors, and risk-conferring behavior.
- I've altered the *Science* cover [shown on slide] (and it is interesting that *Science* discussed this a couple of years ago) to put display those things that I think are of particular importance to CFS: genes, gender (not necessarily sex), and stressors (traumatic, infectious, immune system). These all interact.
- As a result of the items above, CFS is heterogeneous and comprised of subtypes.
- That's why a multi-disciplinary approach is necessary.
- CFS research may help us with other complex, ill-defined illnesses such as FM, post-infectious illness, interstitial cystitis, and multiple chemical sensitivities.

Model Currently Used to Look at CFS – Interactive Biosystems Model

- **The brain** is in the middle of this. I've highlighted some regions of the brain that we now know are involved in CFS as a result of new functional magnetic resonance imaging studies.
- **Stress.** At the simplest level, we can talk about traumatic events during childhood, which certainly are related. We also need to talk about other

stressors, including the concept of allostatic load, which is a biochemical measurement of accumulated lifetime maladaptation to stressors.

- **Genes** are certainly important. They interact with one's reaction to stress. They interact in different manners over time. I am including not just straight genetics, but epigenetics methylation patterns, etc.
- **The autonomic nervous system** is involved in both in heart rate, heart rate variability, and postural hypertension.
- **Immune activation/immune system.** All of what I've mentioned on this list goes in both directions; they are not just unidirectional. Everything that we have seen in our studies of the brain and brain mechanisms are those same mechanisms that are involved in illness when one gets an acute infection. They're also involved in reactivation of latent infections. So if one gets an acute infection, one may get post-infectious fatigue. One may also have latent infections—herpes group viruses are particularly important in this—which may reactivate with various stressors and conditions related to the autonomic nervous system.
- **Diet and lifestyle** are important; again, in both directions. We now know that the occurrence of metabolic syndrome is significantly elevated in people with CFS. It probably goes in both directions, because when one has been ill for a long time, one becomes inactive—it can go that way. It can also go the other way.

CFS Research Strategy

Computation/Modeling

Population studies

- Population studies let us look at risk factors.
- Because our population studies are longitudinal over time and we're now in the seventh year, they allow us to look at the clinical course of the illness, begin to tease out subtypes, and observe different clinical courses and risk factors.
- We measure biomarkers in our population studies. That's part of the laboratory component.
- We can study access and utilization of healthcare and knowledge attitudes and beliefs (KAB).
- We can study economic impact.
- Population studies are what give us participants for clinical studies.

Clinical studies

We do a variety of clinical studies. They are currently in hospital hypothesis testing case control studies. They allow us to:

- Get at risk factors.
- Get at pathophysiology in a very detailed manner.
- Tease out illness subtypes.

- Identify possible pharmacologic or other therapeutic targets.

Laboratory studies

Lab studies cross over other categories. There is nothing we do that doesn't have a laboratory component.

Education

I think that education activities are of particular interest to your Education Subcommittee. Education is where the rubber hits the road. We can do all of this but if people don't know about it—if we haven't changed KAB or treatment patterns, we really haven't gotten anywhere.

2. CFS Logic Model

Why do a logic model? I think that people don't think about them enough. Logic models allow you to put strategy and tactics into perspective with what you're doing. Logic models allow you to really look at what you want to get to and see whether or not you're getting there. We have activities, which are what we do, and we have outcomes, which are what we want to change.

I'll start with the outcomes. They can be short-term, intermediate, or long-term. At the end of all of it, we want to reduce population morbidity associated with CFS and improve quality of life.

What do we do for activities? We have **inputs**, which are our resource platform. It's what we're working from. This committee contributes to those inputs. The **activities** are what we actually do. The **outputs** are what we produce.

Summary of Inputs (Resource Platforms)

- **Significant population morbidity** is associated with this illness. It is not a trivial illness or a trivial burden on society or on the patients.
- **Congress** has realized this and appropriates money to study it.
- **Executive Branch of government:**
 - **Office of Management and Budget**
 - **Department of Health and Human Services (CFSAC)**
 - **CDC**
- **Advocates**
- **Academia**
- **Pharma**

The last three represent people with whom we can directly partner.

Summary of Activities

- **Population surveillance**
- **Educational intervention research**
- **Clinical and laboratory studies**

Summary of Outputs

Population surveillance leads to:

- **Knowing the burden of disease** so we can try to change it.
- **Knowing KAB** of those who have CFS, those who take care of them, and the general population. Once we know KAB, we can see if they're changing.

Educational intervention and clinical and laboratory studies lead to:

- **Clinical guidelines**
- **CFS website**
- **Defining CFS**
- **Risk factors**
- **Pathways**
- **Targets**

The only outputs that we really haven't gotten to yet are therapeutic targets. I think the field is very close to that, there's very promising research, but I'm dealing with our program. In terms of output, between 2000 and 2005, the program has produced 136 peer review publications, four manuscripts that are in press, and ten manuscripts that are in review. Why is this important? It's the way science is done. Research is peer reviewed. If it's not good, it doesn't get published, or at least it gets tweaked until it is good, and then it is published. It can then be vetted by the scientific community, practitioners, etc.

But publications are just publications. What is the impact of the publications? Who have they influenced? Who is reading them? There about 3,000 CFS-related publications on PubMed. There are about 1,600 CFS publications that appeared between 2000 and 2005 that met the Institute for Scientific Information's (ISI) high standards for ISI's rigorous evaluation. The CDC accounts for 5 percent of all ISI-tracked publications.

The only group that accounts for a higher percentage is the combined output of the United Kingdom. All research in the United Kingdom accounts for about 9 percent of all ISI-tracked publications. The New Jersey CFS group accounts for about 5 percent, a similar number to the CDC. The next highest ranking is the combined output of Sweden, which accounts for about 3 percent.

What you really care about is, are people using your research and citing it? Is it coming up in the literature? Has anyone used your stuff? You can track citations. The CDC program has accounted for about 6 percent of all ISI-tracked citations on CFS. Again,

only the combined citations of the UK rank higher at about 7 percent. The next closest is New Jersey with about 3 percent.

Another way to look at it is how often your research is cited. The average CDC article in the 2000-2005 time period has been cited 22 times in the world literature. The next closest citation rate is 18 times. The CDC impact in this area is very, very high.

H-index is another measurement [that is a combination of the CDC's most cited papers and the number of citations received]. CDC's value is 23. The next closest is 15.

Ms. Artman: Scientifically I think that Japan has a huge stake in what they're doing with CFS research, from what I've seen at the IACFS conferences. I'm confused that they're not up here at all.

Dr. Reeves: There are two comments on this. First, this lags a bit. I went back to 2000-2005. It also depends on where someone publishes. When I was working in Latin America, I had a huge number of my publications in the Latin American literature because it's strictly applicable to that. So the Japanese research is moving along very, very rapidly and hasn't caught up on these yet.

What else has our output accomplished other than citations and people using it?

Outcomes – Short-term

One would hope that the KAB of the scientists, providers, and the public have changed. We haven't actually measured that yet. We're in the process of measuring baseline.

Credibility with scientists, providers, and the public is affected by both parts of those. The case definition is a hot topic that is of interest to everybody:

- CFS is a newly-defined illness that was first defined in 1988.
- That CDC case definition was followed by an Australian definition in 1990, then a UK definition in 1991.
- CDC pulled together an international group that met multiple times for about a year and in 1994 published what is currently the international standard for CFS. It has been cited 1,400 times in the ISI-reviewed literature. Any of us who are academicians know that if you get more than about 30 or 40, that's good. This is the reference standard, although it has its problems.
- Beginning in about 2000, we pulled together an international group that met for three years to try to come to some consensus about what was good and what was bad about the 1994 definition. Those became the 2003 International CFS Study Group recommendations. How interested are people in them? They've been cited 69 times. The definition was picked up by ISI as the fast-moving topic of that year.

- And now we begin to get beyond citations. One of the things we try to do is publish in the open access literature so that nobody owns the research. The article describing the 1994 definition has been downloaded about 30,000 times since it was published and is still downloaded at least once a day. The study group recommended standardized instrumentation and development of an instrument validation and publication that measures occurrence, frequency, and severity of accompanying symptoms. We published an article on that in 2004 in the open access literature, not tracked by ISI. It's been downloaded about the same number of times. It has been translated into Dutch and German and used in Germany, the Netherlands, and Switzerland.
- Our most recent attempt to implement the study group recommendations by open access not tracked by ISI produced a download rate that is similar to the 2003 publication.

I think we would all agree that research in CFS by the entire global community has led to an increased number of studies, an increased number of publications, provider KAB that is significantly higher than it was ten years ago, and development of therapies.

3. November 2008 Peer Review

This is an executive summary of the peer review. The report is on the Web, has been provided to CFSAC, and we can certainly make hard copies available. I'm going to use the peer reviewers' comments to frame the rest of the presentation.

Bottom line: they liked the program.

The group was an exceptionally good peer review group. I'm very sorry Dr. Oleske couldn't make it, because I think his opinions would've rounded out some other components.

- Basically, the peer reviewers endorsed the approach of the CDC strategic plan and the logic model to date.
- They did comment on our 2005 publication of the operationalization of the 1994 case definition. This has garnered a lot of attention and an increasing amount of discussion. That's one of the reasons to publish in the peer review literature, so other investigators, etc. can read it, understand what was done, and do studies to either support it or find flaws. That's how you move on.

The peer reviewers' comment was that CDC has led the world in defining CFS. *"While some have recently criticized the recent standardization of the research criteria for CFS, the committee believed that the CDC's work on psychometric operationalization of the existing 1994 case definition should improve the reliability of research."*

Much of what we wanted to do was have measurable outcomes to track treatment trials. We wanted measurable outcomes of impairment, fatigue, and symptoms to try to dissect out subtypes. We wanted something that could be used in research studies to lend some standardization. It is not a rewriting of the 1994 case definition. It's the first attempt to operationalize the recommendations of the international group.

November 2008 Peer Review Strategic Recommendations

Develop a five-year research strategy that integrates current epidemiologic, laboratory, and educational activities of the program and the mission aim of control and prevention of CFS.

This was something that, quite frankly, we had not thought of as deeply as we should have. This came directly from Dr. Boulton and is a reason to have multi-disciplinary peer review groups.

The program should establish closer relationships with traditional public health agencies (i.e. state and local health departments) for the purpose of enhancing both research and education collaborations,

This is going to be a major component of the future for this group, for scientists, for clinicians, and for the patients.

The last recommendation that I will highlight—I've left out a couple that Dr. Monroe had—is the following:

The team needs to consider studies, such as using interventions, that test the direction of causality of pathophysiology.

The biggest flaw with every CFS study done to date is that they are so-called "cross sectional studies" of people who have been ill on for an average of five years. You cannot determine the actual direction of the causality, of psychiatric co-morbidity, of reactivation of infections, etc. if someone's been sick for five years. You really need to do prospective studies.

We're developing a collaboration with the Mayo Clinic to use the Rochester epidemiology database. Ninety percent of the population of Olmsted County, Minnesota, uses the Mayo Clinic from birth to death or for as long as they live there, and their complete medical records are available. We can go back in the medical records and do a retrospective case control study looking at what happened to someone as a kid. Are people who got CFS later more likely to have had a lot of infections? Accidents? Bad asthma or allergies? And then what happens to the clinical course when they get CFS? That is a project that we're just now developing.

April 2009 Stakeholder Meeting

In April [note: slide presentation erroneously cites the meeting as being held in May] we held a stakeholder meeting and the response was very impressive. Given problems with travel, given problems with ill people traveling, given problems with the economy, a fair number of people were there.

- Eight people spoke in person during the meeting.
- We had an open phone line. I counted around 30 people giving comments on the phone, some multiple times. The same person would come back on the telephone to respond to another's comment.
- We've gotten around 350 emails or written comments up to the present. Many of these are the same person writing in once, then thinking of something else and writing in again. Some people have written three or four times. This reflects their interest and concerns and how they really feel about them. It does make it more difficult; however, to pinpoint what percentage of stakeholders feels a certain way.
- We just got the comments from the IACFS/ME group, which we're considering.

April 2009 Stakeholder Meeting Strategic Recommendations

I tried to summarize broad strategic categories of the stakeholder comments. You'll see these as reflecting things that we talked about and that the peer review talked about:

- Communication from the research program, which has obviously not been optimal. We need to improve our communication.
- Case definition – research, clinical, and pediatric.
- Pathophysiology, biomarkers, subtypes.
- Infectious agents and CFS.
- Management and treatment.
- CFS and children.
- Education to help providers, patients, and the public.
- Collaboration and data sharing.
- Funding.

These same types of comments have been raised by collaborators in this country and internationally, by clinicians, and by this very committee. These are, I think, a fair representation of the underlying concerns outside the peer review.

CFS Program Vision Next Five Years

The vision is what it was before—devise control and prevention strategies for CFS through:

- Public health research leading to the control and prevention of CFS.
- Measurable outcomes - does the research make a difference?

When I went through the logic model, the one thing that I did not show are the moderators. It's nice to have inputs and activities, but what about moderators? What about those things outside of one's control?

Moderators can be positive:

- Funding has been quite available to the CFS research program. We could not be where we are without funding.
- Increasing credibility makes people more interested in participating in the field.
- Relevance
- Providers
- Advocacy groups
- Patients

I want to go through the activities that we've successfully done that reflect the positive moderators:

From about 1992-1999, our studies focused on physician surveillance, case control studies, and the first population study in San Francisco. That reflected the funding availability at that time. We had about \$3-\$4 million a year.

Between 2000 and 2005, due to payback funding, we were able to significantly enlarge the program:

- We began surveillance in a large, defined urban population in Wichita, which led to clinical studies.
- We initiated the provider education activities in collaboration with the CFIDS Association of America.
- We did a pilot national survey, which showed us that if you want research quality data, you can't do that.
- We funded one of the best post-infectious fatigue studies in collaboration with the group in Australia.
- We funded some studies of cytokine-induced fatigue, which are actually going to be pivotal to some aspects of infection, reactivation of infection, and some mechanisms of action.
- Based on the population study, we did a clinical study in Wichita.

Currently payback is over and we have decreased funding:

- We did our Georgia cross-sectional case control study.
- Provider education is in process.
- After the Georgia cross-sectional study, we are following that population longitudinally. We have about 5,000 people and we are now into five years of follow up.
- We are doing the GCRC (general clinical research center) study.

- We have initiated a pilot provider registry to patients who are with providers.
- We did a series of quite successful workshops between 2000 and 2002.
- We convened an international CFS study group, which determined that the case definition was the most important. The group also asked if CFS is real. This has just now been published. We funded a study that came out of that of 22 countries, 50 sites, and 8,000 people with chronic fatigue and showed that the construct holds up across cultures and all the regions of the world. The same construct applies in India, China, the Netherlands, South America, and the United States. That basic construct now has a good empiric underpinning. That came out of the international CFS study group.
- We hosted a series of meetings at Cold Spring Harbor to bring the research community together in agreement on the cellular mechanisms of fatigue. How might you model lymphocyte function? How can you go from these markers to models? This was occurring just as the Wichita clinical study was ending, so we had the data.
 - It allowed us to put together the CFS computational challenge. Four teams with members from around the world took that data set and tried to look at it in a way that it hadn't been done before.
 - It led to a dedicated issue of *Pharmacogenomics*.
 - It led to a press conference held by Dr. [Julie] Gerberding [CDC Director].
 - We were approached by Duke University to share that data set in their computational approaches to computational micro array data analysis. They ran that data set for two years. It became very interesting in terms of outcomes because we tracked at least eight publications from groups around the world who never would have touched this sort of data before, getting at some very novel aspects.

Moderators can also hinder:

This is important for CFSAC to take into account and it was very important for the peer review group to take into account. These are times in which economics is a problem for everyone, including the government. NIH also went through this with a period of rapid growth followed by stabilization.

- Before 1999 CDC funding was \$3-4 million per year.
- CDC funding from 2000-2005 averaged \$7.5 million a year. It varied from \$6 million to \$8.5 million.
- Now that payback is over, we are back to stable funding levels at about the same dollar amount that we received in 1999. This represents a 50 percent decrease from the 2003 funding level, which is a 70% decrease in real dollars. It represents a 25 percent decrease in real dollars since 1999. If CDC funding remains level, it will represent a 5-10 percent annual decrease in real dollars.

I'm not going to spend much time on sustainability—it will come up in various contexts. [Slide shows how CDC can spread costs around by participating in various activities.]

To me as an older person, collaboration is working with someone to establish a common goal. It isn't just giving an organization money. It is determining whether we can pool resources to get things done. Pharma is increasingly interested. We've had discussions with some of the other government agencies here. There are things we're doing that are of particular interest to HRSA and NIH and vice versa, so we should be able to come together on some of those things.

CFS Program Five-Year Goals

We were charged to develop a five-year research strategy that integrates current epidemiology, lab, and educational activities with the mission to control and prevent CFS. This is our vision:

We believe that we and other investigators have successfully focused on obtaining the baseline information necessary to plan clinical and educational interventions and to quantitatively/qualitatively measure, at least in our populations, outcomes associated with intervention strategies.

Our strategy is focusing on four goals to plan, implement, and evaluate clinical, educational, and public health interventions:

Goal 1 – Refine understanding of etiologic pathways to improve diagnosis and identify therapeutic targets.

- Identify psychosocial, clinical, and laboratory biomarkers associated with the clinical course of CFS and with subsets of the illness.
- Identify risk factors associated with subsets of the illness. I will cite a non-CFS illness—major depressive disorder—as an extremely good example of what I mean. There are at least two big subsets major depressive disorder that have quite different risk factors and quite different responses to different therapies.
- Improve our focus on measures of the neuroendocrine, metabolic, immune, and infectious characteristics of CFS to identify targets for the various subsets of the illness.
- Elucidate pathophysiologic mechanisms.
- Develop collaborative data sharing networks to extend knowledge concerning CFS. Those are networks that would be much like the international study group.

Goal 2 – Improve clinical management by providing evidence-based educational materials addressing evaluation and clinical management.

- We are planning an international consensus meeting regarding diagnosis of CFS in research and clinical settings.
- We are planning an international consensus meeting regarding management and treatment of CFS.
- We need to get current evidence-based information on diagnosis and treatment out to those who need it.

- We need to evaluate things we've measured in the population including the effects of access, utilization, and quality of healthcare on the clinical course of the illness.

Goal 3 – Improve diagnosis and management through research.

- We need to establish an international CFS research network. We'll be putting together another meeting—it will probably be in 2010—of the international CFS study group. We obviously have to look around and see who's interested, who's productive, and who the stakeholders are. These are not one-shot, one-day gatherings. They usually lead to a lot more.
- We need to collaborate to conduct clinical intervention trials. We are discussing several of those.

Goal 4 – Move CFS into the mainstream of public health concerns.

- Develop collaborations with national, state, and local public health authorities. We're beginning to do that much more seriously with our CSTE fellow, with our EIS fellow, and with local and state health departments.
- Provide evidence-based information to institutional authorities.
- Evaluate outcomes associated with dissemination of public health information. If we put it out and nobody reads it, it didn't make a difference.

4. Activities and Milestones

Workshops and International Research Networks

- International Workshop – Clinical Management of CFS. I haven't sent the emails yet, but we're hoping to do it by September or October. Comments from this committee discussing such a workshop would be appreciated.
- International Workshop – Research, Clinical, and Pediatric Definitions of CFS - I would like to try to get together by the winter of 2009. I know the IACFS/ME is interested in this. We want to include countries such as UK that have CFS care completely integrated into their healthcare system.
- International CFS Study Group – Identify Research Priorities. We need people from countries that have successfully done it to help identify research priorities.

Surveillance

- CDC is doing longitudinal studies of a random selection of the population of metropolitan Atlanta, urban Macon, and rural Georgia. We are now into the fifth year of follow up. About 80 percent of the people continue to participate.
- We are initiating a CFS provider registry that will also be longitudinal. It is a defined population, so I can extend it to other defined populations and compare it with people who are getting care. It allows us, with efficient use of resources, to get research quality data. We do a telephone interview, then bring people into a clinic to do very sophisticated measurements.

You can measure the effects of educational interventions if you're measuring KAB, duration of illness, clinical course, and accessing healthcare. You can measure the effects of public awareness messages on the population.

What's the biggest weakness of these studies? You cannot *a priori* generalize from Georgia to the entire United States. What we can say is that this data does represent metropolitan and rural populations in Georgia and it's got a high racial/ethnic minority population, but I can't extend results to Washington, New York City, or Wichita.

The Georgia data does, however, serve as a proof of concept. It serves as a comparison for researchers in other locations. For example, Dr. Jason can say, "I saw some things in Chicago; do I see that the same things apply in metropolitan Georgia?" As other groups begin to do this, the proof of concept can occur. Economics is another example. Dr. Jason has measured economics in Chicago using slightly different methods than we have, so we're able to compare different methods, different research groups, and different populations and see what the commonalities are nationally and internationally.

One of our hopes is that as this happens, it will help people to focus on what might be the core variables that one needs to have and how one might go about getting them. If a group is a consortium, are we all collecting the same kind of variables that can be looked at in the same way?

- Mayo Clinic Rochester Epidemiology Project

Clinical Studies

- Emory University GCRC Study. We are evaluating 30 CFS cases and 60 sex/race/age/ body mass index-matched controls. We're looking at brain function in two days of fMRI studies as related to cognitive function, and we're measuring metabolic and autonomic nervous system functions in reaction to a social stressor. That study will be over patient enrollment in July. We are seeing differences in the frontal, cingulate, and basal regions of the brain lighting up. We're seeing differences in hypothalamic-pituitary-adrenal (HPA) axis activities,

and we're seeing some interesting differences in autonomic nervous system activities—separations of parasympathetic and sympathetic.

- CBT GET. We are in the process of planning a cognitive behavioral therapy (CBT) and graded exercise (GET) trial as part of the provider registry population in Macon. We're going to do that in collaboration with the providers in Macon, with Mercer Medical School, with the U.K. group, and with Mayo Clinic. Obviously, CBT GET is not the cure for everybody. Nobody knows for how many it is. It probably applies to a subset.
- Pharmacologic trials. We hope—in part based on interest by pharma, collaborators, and what might come out of some of the research meetings—to begin some pharmacologic trials, either by ourselves or in collaboration. We're discussing collaborating with Hemispherx in the trial that they have going.

Laboratory Studies

Laboratory studies are part of everything. This slide is just to demonstrate the range of wet lab markers. I look upon FMRI, polysomnography, and electrophysiology as lab markers. [Slide includes plasma, serum, peripheral blood mononuclear cells (PBMC), hormones, metabolites, active hormones, and Circadian rhythm.]

Educational Intervention and Research

The laboratory component is very complex. You're always publishing several years behind. We did a great study in Wichita. We got some great things out of it. It made some differences. But it takes a year to physically do the study. It takes up to a year to actually finish lab testing, sort out the data, and then figure out what it means.

The education component is where the rubber hits the road. All of those other things have to come together to get into it. There's a fairly extensive discussion of this in the draft plan.

- We operate a CFS website. I talked about that the last time I was here. We have a very active research program analyzing use of that website, which is being redesigned. The new design comes out imminently.
- We have a provider CME program that we are in the process of updating.
- We are going to initiate a provider education intervention in Bibb County as part of the registry activities.
- I've already mentioned our new relationships with public health agencies.

Committee Discussion

CFSAC members discussed amending the meeting agenda because only seven minutes remained to discuss Dr. Reeves' presentation. Dr. Jones noted that with eight

members of the public waiting to testify, the upcoming comment period had to proceed as scheduled.

Committee members agreed to take a five-minute break, proceed with the public comment period, adjourn briefly for lunch, then return to dialog with Dr. Reeves rather than take the scheduled Subcommittee Lunch.

Dr. Cavaille-Coll: FDA has to make a comment. As we see the evolution of the case definition of CFS, people need to know that that's going to affect drug development because clinical trials that are based on older definitions will not be applicable to the new definitions. I think we need to be mindful about how we are changing the definition of CFS because it does affect FDA's ability to make decisions about clinical trials for that particular disease.

We do recognize that most of the symptoms of CFS are already managed by products that are already lawfully marketed. But if we want to have products that are indicated specifically for CFS, we need to make sure what the case definition is. I feel like I had to say this right now because I have seen over the last 15 years a change in what people are defining as CFS.

[Dr. Oleske called a five-minute break.]

Public Comment

Dr. Jones reconvened the CFSAC meeting and read the list of public commenters. She explained that all presenters had been apprised that they were allotted five minutes each to make their remarks. Dr. Jones said that a timer box placed on a table in the middle of the hearing room would show green when a speaker was within the five-minute allocation and yellow when the speaker had one minute left. A flashing red light would indicate that the five-minute allotment had passed, and after five minutes and 30 seconds, Dr. Jones said that she would turn off the microphone.

She explained that there is much demand for public comment. CFSAC tried to honor all of the requests made by expanding the time allotted for these comments.

Pat Fero, Wisconsin

Accompanying Documents: *Chronic Fatigue Syndrome Budget, 5/21/09; Fibromyalgia Budget; Research Project Grants—Success Rates of Competing Applications by Application Type, NIH Institutes/Centers and Activity Code, Fiscal Years 2008-1999; Research Disease Areas (funding); 3/10/09 FOIA ONE: CFS SEP Peer reviewed Awards FY 2007-2009 NEW; FOIA TWO, data drawn from frozen files accessed on 3/10/09; Freeman, Roy, Professor of Neurology, Beth Israel Deaconess, Orthostatic Intolerance in CFS, HL059459-09; Behavioral Insomnia Therapy With Chronic Fatigue Syndrome: CARNEY/KRYSTAL DUKE 2007*

NR010539; NIH Competing Research Project Applications: Fiscal Year 2008; Fibromyalgia: 2009 ALL Fibromyalgia non expired grants

I have a thumb drive if anyone wants to download this information onto your computer.

I'm going to go through these charts quickly. I think we have a crisis here in funding. We all know this, but we can tell by this abbreviated report. The sources are always in the top left hand corner so you know where I got all of this information. I have three sources of information in this report.

You can see \$3 million projected for CFS next year. I think that's equal to 1994—I didn't check this out specifically, but I think that's at the '93-'94 level, maybe even less than that. I also highlighted FM, which is going up to \$13 million.

I included the chart on success rates along with how those rates were calculated for 2008, because researchers are always talking about the success rates. We'll see later on about success rates, but there are a number of items to consider that you might not have taken into account when I come to some conclusions later on.

If you look carefully at the Research Disease Areas sheet under Musculoskeletal, Oral and Skin Sciences (MOSS) Scientific Areas of Integrated Review Groups (IRGs), you'll see there's a red item under each one except under CFS/FM Special Emphasis Panel (CFS SEP). We don't have collaborators. If you look carefully at this sheet, you'll wonder who's with us. I suspect, as many of us believe, that we really don't have a home. You'll have to look at this more carefully. I don't have time to go through it.

The next chart is simply a glossary. We know that grants come into CSR (Center for Scientific Review). They're logged in somehow. They go to what's the most appropriate review group, and then they're assigned an IC (Institute or Center) code. The ICs actually award the money. The CSR doesn't have anything to do with awarding money, but they review grants.

FOIA ONE—CFS SEP Peer reviewed Awards FY 2007-2009 NEW – this differs from the second FOIA because the grants are peer reviewed. I wanted to know by Council round how many were reviewed, how many actually made it onto Council, and how many grants were awarded. You can see the totals on the right hand side. It's important that I point out why I have outlined the two in light green—under Principal Investigators Krystal and Freeman. I did not count them because of the following two pages (grant abstracts).

I've tracked Roy Freeman for a number of years. He may be a wonderful scientist and doctor, but nonetheless unless it's very, very recent, he hasn't published on CFS since 2002. Here's a statement from his background in the abstract—he was just renewed at \$412,000. He's had the grant for 11 years—orthostatic intolerance in CFS. I do not understand why he was renewed when he's not doing anything with CFS. You can go to his website; you can look at his publications. Nothing's there.

The next one is the Carney/Krystal. You'll have to read this in detail. If you look down at the bottom, this is a behavioral treatment for insomnia done at Duke University. I wanted to be in that study, so I requested by email. I was denied due to other conditions that I have. They're using the National Institute for Health and Clinical Excellence (NICE) guidelines and the inclusion/exclusion Reeves criteria from 2005 (they incorrectly cite it as 2003) in order to recruit subjects and exclude patients. They've published nothing. They're interested in behavioral insomnia treatments for schizophrenia, bipolar, FM, etc. They're not interested in our population.

Caroline Fribrance, President, *Wisconsin ME/CFS Association*

I was here last October requesting that these meetings be made public on the Web for our many members who can't be here, so I want to thank those responsible for making the web cast possible. I would have liked to see this happen a long time ago, but I'm not blaming those who did it now for that. We had no time to let our members know so they could watch it simultaneously but I'm happy to hear that's it's going to be archived and will be available to them.

I wanted to talk just briefly about the question of reasonable accommodation. I'm not precisely sure what it means at HHS for a meeting like this. I'm very much aware of what reasonable accommodation means in the employment context. I have to tell you that I can't believe that there isn't a couch or an easy chair or even a chair that couldn't be moved into this screened area for people who become fatigued at these meetings. Or that there's not a couch somewhere in this building that for four days a year could be in that screened section.

Last October I became overcome with fatigue at about two o'clock in the afternoon, took my pillow, and went back there and laid on the floor. Unfortunately, I suffered a lot of aches and pains afterwards. I would think that HHS should be a model of reasonable accommodation, and I just can't quite believe that this is what's considered an accommodation.

To move on, I wanted to say something about CDC. It's probably been said before. I'm not sure what Dr. Reeves meant when he said that they got comments on communication, but my guess is that he might have heard that there was not sufficient notice of the meeting. I for one would have loved to have gone to Atlanta, but two weeks is not enough to clear my calendar, make sure I'm going to feel well enough, and get there. I'm sure that's true for others. It strikes me that that's not a bonafide effort to include stakeholders—to give them about two weeks notice about a meeting like that. Yes, I realize that I could have phoned in, but I'm someone who likes to prepare remarks, and two weeks did not allow me to do that. I will be submitting remarks, but my point is, that's not how you do it if you really want to hear from people. I consider it a slap in the face.

I also want to comment on what he just reported on. It all sounded very nice but it seems to me that he's reporting on things that needed to happen a long time ago. I'm familiar with some of the funding facts that Pat has referred to. I have a background in epidemiology. I've been watching CFS research for years. I go to the international conferences, and it's pretty clear to me that the kinds of things that get funded and get called CFS research are often not and they're often not by people who are involved with CFS and are knowledgeable about CFS. I guess I'm echoing some of Kim McCleary's comments.

It seems to me that with the very few resources that we have these days, they need to be directed particularly, finally, at the most important questions. I see this money going to people and places and subjects that are far off the mark of what I think patients would really like to see. While there was a lot that was admirable in what was presented, it's too little too late and needs to be far more focused on the things that are most going to help patients.

Dr. Oleske: We'll try to accommodate back there. We'll look into that so that there is a better facility for people who are here.

Dr. Jones requested that those testifying avoid cupping their hands over the microphone because it causes feedback for both the web cast and audio recording.

Mary Schweitzer, New Jersey

Accompanying Document: *The Orwellian NewSpeak of M.E. and CFS Studies*

I want to thank you for allowing me time to speak. I also want to thank Dr. Jones for the welcoming atmosphere when I showed up. There were really kind people downstairs who were ready for us, had names tags for us, and brought us up here. Then this wonderful live stream video. This is just wonderful for all the patients out there who would like to know what happens here and have always wanted to see it in real time. Thank you very much from the bottom of our hearts.

I haven't been doing very well. I've been wearing sunglasses most of the time because these lights really hurt my eyes, and I was back there lying down. I need to catch everybody up with how my case is going. Fifteen months ago I lost Ampligen. A year ago I testified that I was terrified of what was going to happen. I started to relapse on Labor Day and suffered the return of many symptoms, among them: a VO2 max score of 16 (that alone would give you disability), reactivated Epstein-Barr virus (EBV), human herpes virus (HHV) 6A, 37-kD RNA cell factor, a low natural killer cell count and function, cytomegalovirus, decreased activity in the left lateral temporal lobe and occipital lobes, and an abnormal halter monitor test probably related to the NMH (neurally mediated hypotension) POTS (postural orthostatic tachycardia syndrome) I'd known about for a long time. I've had months of a low-grade fever and headaches, I can't drive because I get confused, and I have problems with short-term memory. I lay in bed in the dark. My husband gave me a Blackberry so I can keep up with email. But he doesn't like me to do that all of the time. He'll throw me in the wheelchair and take

me to a baseball game twice a week so he at least gets me out to something that I enjoy.

I consider myself lucky because I do have a family; I do have a support network. My family knows that whatever it does for other people, Ampligen was what was working for me. My daughter sent me a bouquet of flowers for Mother's Day and she wrote on the card, "I wish it was a bouquet of Ampligen, Mom. I can't do that for you." And I'm somebody who has resources. What does somebody do who doesn't have a family to take care of them? Where do they go? If I didn't have a family, as sick as I am, I would be sleeping on grates out there. I would be homeless.

I'm going to have to shift gears now because of Dr. Reeves' testimony. First of all, this new definition—I'm not in the new definition. I would not fit the new definition. Neither would the people in the Incline Village cluster outbreak. Shouldn't a diagnosis at least fit the people it was designed to describe? This new definition is really, really bad. It takes out the people who are really sick and it folds in people who have mental problems. So the people you are going to be studying aren't the people that you're supposed to be studying, and I can't emphasize this enough.

When they talk about cooperating with the UK program, that's psychiatrists. And let me give you a direct quote from Dr. Peter White, who is a major contributor to all of this. According to an article by Dr. White in a 2002 journal, "No physical treatments for CFS or ME were supported by two recent systematic reviews of the management of both conditions." Obviously he hadn't read anything written by Komaroff. "The only two treatments that showed promise are cognitive behavioral therapy and graded exercise therapy." CBE and GET are in that second set of papers that I gave you.

Dr. White continues, "Although neither treatment is based on the understanding that CFS is psychological, both treatments were developed and tested on a biopsychosocial understanding of the disease. The common principle is the gradual return to avoided activities. Even the physical or biological treatments often use psychiatry such as antidepressants to treat CFS. The disease is caused by too much rest leading to de-conditioning and anxiety about illness. The more one worries about a symptom, the more one focuses on it and the more stress this generates, which in turn worsens the symptoms."

Peter White—that's who is doing the consulting for the CDC. That is who is behind this new definition. Get rid of the definition and burn the questionnaires—that's number one in my set of goals. Other people would support similar goals:

1. End the current CDC program on CFS now and burn the questionnaires.
2. Return to the goals of the 1994 Fukuda study. Dr. Reeves was talking about it but he wasn't doing it—go to objective biomarkers.
3. Abandon the psychosocial approach and do not hire British psychiatrists as consultants to the CDC for my disease. It is not psychological.

4. Make public the testing and treatment that those of us who pay cash are getting so that others have a chance at treatment and diagnosis. The easiest way to start is to look at the Canadian protocol.
5. As for equitable funding for our disease, adopt the WHO diagnostic criteria and recognition of myalgic encephalomyelitis in neurology. HHV encephalitis now has its own code. You might want to tell physicians that. You might want to read a report that a group of us wrote for the Obama transition team that has been put on the healthcare.gov website.
6. And finally, centers of excellence. Centers of excellence.

Meghan Shannon, *New Jersey*

Accompanying Documents: *What is ME? What is CFS? INFORMATION FOR CLINICIANS AND LAWYERS, December 2001; Codes Used for Adjudicating Chronic Fatigue Syndrome (CFS) Cases, (Per Our Telephone Discussion of January 31, 1995)*

I started the medical professionals group across the United States. I've been a part of *Our Bodies, Ourselves* and the women's health groups. I would like to say that CFS is a misdiagnosis of a disease that is in process. Nobody in this room has CFS because there is no such thing as CFS. It's ME or post polio or cancer. I was misdiagnosed from the beginning. There is a packet that I gave to Dr. Oleske discussing what is ME and what is CFS. This is out of the UK. These are the doctors who are researching ME—Dr. Malcolm Cooper is a hero.

As far as education is concerned, Dr. Lee, at the end of his tenure, did have the CDC put together a public health interactive satellite video conference that got completely hijacked by the AACFS (American Association for Chronic Fatigue Syndrome). For some reason it was not available to doctors in the US so that they could get continuing education. This is an incredible way to get education out to the doctor's. It's been tried before. This was in 1997.

As far as the coding is concerned, I have given you something that I pulled out of my bag of tricks that I have from 1995. I got a letter from Carolyn Kiefer who used to work at SSA and was the representative to CFSAC. This is critical to know that SSA tried to list a code—668—to pull out anybody who had fatigue syndrome. What they got was AIDS patients, cancer patients, and all the autoimmune disease patients because every one of those people had fatigue as their major problem. That shows that back in 1995, SSA did try to tease out CFS and they couldn't. They failed at it. The diagnostic codes used at the time were immune deficiencies, endocrine disorders, multiple sclerosis fatigue issues, affective disorders, and nervous system disorders. The critical thing about it is that it was tried using the word "fatigue," which is why we need to get rid of that. People can be rediagnosed with immune disorders or neurological disorders. You don't need to have a code for CFS because there is no such thing.

One of the things that I was reading in my paperwork is that the late Dr. David Purtilo, who developed the original 1988 definition, opposed CFS. He was actually more in

favor of ME. He wrote a lot of research papers about chronic EBV and CFS and cautioned researchers back in 1988 to think about whether they were studying chronic EBV or CFS. If researchers are taking in only people with certain viruses, they are not studying what's known as CFS. We still don't know what CFS is. That's another reason to let go of CFS. Go to where there are codes; to where there are disease processes that we know about. This is not new.

I am in the study of the late Dr. Purtilo because I have a twin sister. I am in three different twin studies. My blood profile is profoundly different and we are identical. I have no EBV. The only herpes virus I have is herpes zoster, and it just shows that I worked in a hospital. My sister was consistently labeled the "sick twin" because she shows high titers to EBV in Dedra Buchwald's twin study. We left that study because they kept putting me in as the well twin and my twin sister as the sick twin by using EBV as one of the markers.

Dr. Alan McCutcheon, who was a well-known AIDS doctor like Dr. Nancy Klimas, was the first one to ever, ever give me respect. He did the CD4/CD8 ratios on me and it turns out that people who are exposed to polio have the same defect that AIDS people have in the CD4/CD8 ratio.

Dr. Jones: Your time is up.

Ms. Shannon: It's not enough time.

Dr. Oleske: Thank you again. By the way, while the next person's coming up, if someone has a solution for this short five minutes let me know. We want to get as many people in as possible.

Heidi Bauer, *Maryland*

This is my first time at attempting any kind of advocacy. I do appreciate your allowing me to have some time to speak, though.

I've chosen to speak today about some personal experiences with CFS, especially as a mother raising small children, and about some sad situations that I see for my fellow CFS sufferers. My purpose is to remind those involved at the CDC that there are faces behind the statistics and there are millions of us crying out for scientific validation for the conglomerate of symptoms we experience with CFS.

This Memorial Day weekend was the most memorable I've had in 13 years. I attended a Blue Angel show with my family and organized our first family picnic. I was actively participating in public and family life. Two days prior, I was sick in bed for three weeks dealing with autonomic issues from CFS and widespread pain from FM. My brain felt like molasses. I was unable to work on this speech and feared I would miss out on a great opportunity to speak.

It astounds me how these symptoms can magically disappear sometimes. But I do what most CFS sufferers do. I was proud that I was able to accomplish so much that some take for granted. You'll hear us report being able to do the simplest of tasks like, "I planted some flowers today. I got a load of laundry washed," or sadly, "I got a shower today, dressed myself, or ate." We normally focus on the positives and appreciate what we've been able to do despite our pain, dizziness, nausea, brain fog, and fatigue, and rightly so. But when the time comes for us to tell SSA why we're applying for benefits, we are faced with some difficult realizations as to what our normal days entail.

I found out when my children were two that I was only caring for them 20 waking hours a week because I was too ill to even care for their basic needs. Some people with CFS have asked me why I chose to have children despite being diagnosed with CFS and FM. The response is, in a nutshell, misinformation. In 2000, I searched the Internet for information about CFS and having children. I found nothing. I looked for information about how long CFS lasted for most patients. I kind of laugh at these studies now. I stumbled on three different articles that said a third of patients recover after five years, two-thirds after 10 years. Since I was at the five-year point and was in an upswing with symptoms, I thought that perhaps I was one of the lucky third who would stay well.

Unfortunately we discovered that we needed help getting pregnant. As the fertility hormones took their toll on my body, I told my husband I would try one more time. I was starting to seriously doubt that I was going to be one of the lucky third. We were blessed with a set of health triplets in August 2003. I'd do anything for them, including becoming an advocate for my health—and with the familial aspects of this disease—potentially their health as well.

It's been difficult, though. The only way I have managed is through a large amount of financial and physical help from my family and organization habits left over from the days when I was an English teacher. I would like to see the CDC create more information for women with CFS concerning pregnancy and childrearing. Women should know how this might affect their symptoms so that they can make an informed decision. The cost of childcare should be addressed as well as the emotional difficulties created by the limitations CFS imposes on parents. A mother with CFS often misses out on many of her children's firsts, has difficulty helping them with school, and cuts out many activities because she does not have the energy to drive them. It can be depressing.

When I get weary of my struggles with CFS, I turn to the online communities. In the introduction section of each community, you will often find all the details about people's experiences with CFS. You'll see how many years they've suffered, their experience trying to get diagnosed, and some lucky ones are able to post blood test results documenting viruses and killer cell counts. It struck me one day just how much we need validation that we are ill, even with each other. We grasp at any piece of the puzzle through tests and doctors to remind us that we are sick, and not just lazy or depressed. We wear our validating sign as a badge to all non-believers. "See? Here's proof." For me it's also a reminder to myself. There are days when I feel relatively

healthy and I wonder, maybe if I just push myself harder I'll find that I'm not as sick as I think I am. A couple days later, stuck in bed again, I'm proven wrong.

Often with a relapse, we try again to find a cure for our weak and sore bodies. Disgusted by the way Western medicine seems to have let us down, we turn to alternative therapies. I personally hold the belief that some of these therapies might help CFS. The general feeling I get is that most people with CFS find little to no help with them at this point. Despite that, claims of curing CFS patients are advertised by certain doctors who are more like snake oil sellers than authentic, well-trained neuropaths. Our desperation makes us vulnerable to their claims, and much-needed savings are wasted in the pursuit to regain our health. Until the root cause or causes of CFS are found, we are sitting ducks to snake oil sellers touting their remedies.

While it saddens me to find the CDC has not made more significant strides in the last 20 years, I'm hopeful the advice of doctors, scientists, and advocate will not go unheeded by this committee, and the CFS community will have full access to accurate, well-researched information that will empower them to make the right choices for their bodies. I also hope that taxpayer money will be handled wisely when funding research programs so we no longer have to grasp at straws in order to validate that we are ill.

Thank you for your time.

Cort Johnson

We are in the middle of the CDC's ten-year review. I applaud the CDC for the review process. However, I look forward to participating in the ten-year review of the research arm of the Federal government—the NIH—at some point. Patients across this spectrum are understandably upset that little has been done in the past ten years to assist them with this disorder. We have watched decades of their lives lost in the wasteland of fatigue and pain they do not understand and can find little relief from. They've seen doctor after doctor in a fruitless search for wellness.

Much of their anger has been focused, rightly or wrongly, on the individual investigators. I would argue, though, that the real culprits in this story are not researcher X or Y, but the people behind the scenes, mostly unknown to the ME/CFS community, who have decided that no matter what its consequences or how many it affects, this disease is not worth significant funding. Whatever the failings of any individual researchers, they pale beside the almost criminal disregard shown by the Federal agencies to the sufferers of this disorder.

One wonders how the CDC personnel get the audacity to get up before an audience of suffering patients as they did during the CDC comment session last March and say that they care. One wonders what that brave CDC staffer who went public with her struggle with ME/CFS thought of CDC personnel using her story as proof that they are committed to assisting people with ME/CFS when they are spending, based on their own population estimates, a dollar a year on each patient. If CDC estimates are

correct, the CDC is spending pocket change on a disorder that affects about 1 percent of the population. This indicates to me that nothing has really changed in the last ten years and suggests that the Federal government in its heart of hearts still believes that CFS patients are malingerers. I can't find any way else to explain spending pennies on a disorder that has 25 percent disability rates and costs \$25 billion a year in economic losses. Statistics like that make me believe that the Federal health agencies are not data driven, objective, scientific organizations at all but good old boys clubs riddled with superstition and ad hoc reasoning.

If the CDC or NIH were driven by data, then data like that would call for some action. Instead of increasing funding as the estimates have gone up, both agencies have cut funding dramatically. In fact the only message that one could conceivably get from the program at the ORWH is that not only is the NIH not committed to this field, but they would be happy to see it die. I ask you why, given the record of the ME/CFS program at the ORWH—three research centers closed, one conference in the last eight years, one small RFA that was only a quarter funded, an over 50 percent decline in funding, and an 8 percent new grant acceptance rate—any researcher would even think of entering this field. You don't need to cut a program to allow it to die as a viable entity. All you need to do is watch it go down the drain.

Because the NIH has done virtually nothing to build a struggling field, it appears that the biggest funding boost in the NIH's history will pass like a mirage in the desert for ME/CFS researchers. Almost ten years ago, the NIH moved the ME/CFS program to the ORWH, which has turned out to be the equivalent of sending it so Siberia. They gave the ORWH, despite the efforts of the personnel at the ORWH, nobody to run it and counted on other institutes, none of which has any responsibility for this disorder, to fund it, and they have failed to do so.

This has turned out to be incredibly naïve. In the last five years, the budget for CFS research has tumbled 50 percent, the highest funding loss of any disease that the NIH funds, and the NIH has done nothing to stem that. I say to CDC and NIH administrators that your words are empty. That with your miserly funding, you have turned your backs and continue to turn your backs, on an enormous number of suffering people. The CDC should be more than about controlling the diseases that they want to control. The NIH should be more than about defending the health of the people that they want to study. Both organizations should be more than about furthering the career paths of their investigators. They should have the guts to tackle the messy problems as well. The fact that people are suffering should count for something.

Thank you.

Robert Miller, Virginia
Accompanying Document: *Written testimony*

Thank you for allowing me to give my testimony today and thank you for web casting this meeting.

My name is Robert Miller and I am a CFS patient. I have remained ill for over 20 years due largely in part to the complete failure of the CDC to do its part for the patient population.

CDC stands for Centers for Disease Control and Prevention, of which it has done neither—control or prevent this life-destroying illness. I am for the most part chained to my house due to CFS and I depend upon my wife and two eight year-old sons.

I put my trust and faith in the CDC to move CFS research forward in a timely manner much in the way the NIH had done for my deceased sisters who were born with cancer over 45 years ago and my elder brother, who died from testicular cancer after a nine-year battle. All of them took part in cutting edge research and treatments, my sisters in the 1960's at Sloan Memorial Hospital—a true “Center for Excellence”—and my brother at Baptist Hospital in Miami. Those cutting edge treatments benefited my sisters as well as the thousands of children who came after them, and it gave my brother nine years of life, allowing him to see his daughter graduate.

I believe I am doing my part to further the science along in CFS. I have given blood, muscle tissue, spinal fluid, and a lymph node to further along research in CFS. I volunteered in two FDA-approved drug trials to test treatments.

And with all due respect to this committee—and I am humbled by your dedication to help us all with CFS—I believe it's time to make very substantial, “life-changing” recommendations to the new Secretary of Health for the million patients like me who have faced the same stonewalling by our Federal agencies for 25 years.

First: You will hear today about the CDC's “CFS Strategic Research Plan.” I'll tell you what I told the CDC at their April meeting: no matter how much money is allocated to this program, it will fail until the head of this program is changed. We need to attack this illness with a new attitude and a new commitment. We need to do what is best for the CFS community and replace Dr. Reeves as the head of this program.

I am appalled by Dr. Reeves' lack of urgency and leadership, not just this year, but for years past. I have attended CFSAC meetings in which Dr. Reeves does not have the respect nor decency to stay and listen to the testimony of CFS patients, who have sacrificed much financially and suffered physically just to attend to give a five-minute testimony. When it's time for those public comments, Dr. Reeves runs out of the meeting. Recently I attended the 2009 IACFS conference in Reno where top researchers, doctors, and patients from all across the globe gathered to present, share, and listen to the latest science and research on CFS/ME. Dr. Reeves was not there.

How can this happen? How can the head of this program not attend one of the most important conferences being presented? How can he not be presenting? This is a total failure. We need the CDC to have a CFS program leader who can think out of the box

the way the CDC was forced to do with HIV, and that leader needs to be dynamic and energetic with a sense of urgency matching the needs of our CFS community.

Second: Funding must be a top priority at the Federal agencies. Leadership has changed. New leaders who actually believe in science have a mandate to make change, but they need you—the only Federal board of experts on CFS—to call for bold investments quickly. We need you to make the following recommendations to the new Secretary of Health:

- Require HHS agencies to budget \$100 million in the first two years of the new Administration to CFS research.
- Require NIH to fund 50 percent of the grant proposals submitted to its institutes until it reaches a meaningful funding level.
- Require CDC to provide access to its vast store of data to all CFS researchers and clinicians worldwide.
- Direct the FDA to approve Ampligen, the only drug to complete Phase III FDA-approved trials that have shown efficacy and safety. After more than ten years of late stage study, yesterday, once again, the FDA stalled the approval. To quote the agency, “The delay was attributed by the agency to certain staff scheduling changes which might (or might not) delay the report.”
- Require the FDA to solicit applications for CFS treatment.
- Call for Federally-funded centers for excellence devoted to CFS. There is such a center being built as we speak with private and state funding. Federal funding would slingshot this center into results for us all with CFS. It is The Whittemore Peterson Institute in Reno.

We would not be able to say today that we can cure or treat many cancers without centers like Sloane Kettering and the National Cancer Institute. The CFS community will not be able to celebrate diagnostic markers, treatments, or patients...

Dr. Jones: Your time is up.

Mr. Miller: ...returning to work without sophisticated centers of excellence. Thank you.

Dr. Jones: Kim McCleary is the last commenter for this comment period. I would note that we do have another public comment period scheduled for 4-5 p.m. today and another one tomorrow as well.

Kim McCleary, President and CEO, *The CFIDS Association of America*
Accompanying Document: *Written Statement to the Department of Health & Human Services Chronic Fatigue Syndrome Advisory Committee Submitted May 22, 2009*

I submitted written testimony that I'm going to divert from. Since you all have it in writing, I'm not going to bother reading it to you. It does address some of the issues that others have spoken about in terms of the magnitude of the illness, the opportunities

under the Recovery Act, and some of the ongoing CDC issues. But I thought that in light of the CDC's presentation of its strategic plan, I would focus my comments towards the committee, since you will have the opportunity to more thoroughly question Dr. Reeves, Dr. Miller, Dr. Monroe, and Sarah Wiley this afternoon. I will try to bring up some issues that I felt as an observer were important in terms of understanding where CDC is going.

I came here hoping to hear a focused presentation on what the future of CFS research will look like at the CDC and instead, I was disappointed that we got a history lesson that I think most of us in the room recognize from past sessions. One of the central topics seems to be a lack of clarity about where the mission of NIH begins and ends and where the mission of the CDC begins and ends. A lot of the studies that were included in that presentation sound like they would be responsive to the NIH's neuroimmune PA.

My understanding of the way HHS is constructed and the agencies work together, they should be complementary rather than overlapping. This has been a discussion topic since the blue ribbon panel was convened in January of '07: How much of what CDC is planning to do is appropriate to the mission of the nation's public health agency and how much of it would be better placed at NIH to be done in academic centers?

The long-term history of the program going back into the year 2000 and before is helpful, but I think that looking back over a decade obscures how little has happened in the last two or three years. I hope that the committee will focus on the more recent past rather than the distant past. And while it can be helpful to have a continuous theme of this vision and a strategy and the operational definitions that are being used to make those pretty box charts, I'm deeply concerned that it also represents stagnation, that there hasn't been new thinking and innovative ideas go forward in light of the new technologies that are available to us, what other people in the field are doing, and what the broader community now sees as consensus issues in CFS research.

A lot has been made of the empiric definition. While it continues to be clarified that this does not represent a new definition of CFS, I think that most people would agree at this point that it circles a different patient group than the '94 utilized in a more traditional way without the instruments and the cutoff points that have been established. If CDC continues to use the empiric definition and everybody else in academia, around the world, and in pharmaceutical and biotech companies uses the '94 definition without those same instruments applied, I think that Dr. Cavaille-Coll is correct—it changes everything. It would make things totally incomparable. We won't be able to compare one thing to the next.

CDC represents at least half the CDC funding in the United States, and worldwide, it represents probably a third to 40 percent of total spending. Does that mean we can't even bring that set of research findings into the larger whole? I think that's something that this committee has a unique ability to help sort out, because the other agencies of HHS are not using the same definition or the same measurements to define CFS as the

CDC is. Subsets of the disease were discussed, but there was no mention of how they will be consistent among agencies.

The plan mentions education interventions that are going to be used, but absolutely no discussion of what plan there is to broaden or generalize those findings. Dr. Reeves himself had said that you can't generalize Georgia to the greater US. What does that mean when you get to the end of those studies?

Last, I would note that he discussed at the very beginning of his presentation that CFS has the same symptoms and systems as conditions that begin with acute or reactivated viral infections, yet there's no mention of those types of studies in the plan looking forward.

I think the committee should clarify what the priorities are, what the emphasis is, what the staffing and expertise levels are that can get this work done, and what the budget is. Is it budgeted based on what they've been getting or is there a new budget idea of how much it will cost to do this research? I hope that we can pare down through those questions about this kitchen sink plan that's got a few popular items thrown into it and have a better idea of exactly what's happening moving forward.

Dr. Oleske: We're going to take a break until 1:15 p.m. to grab lunch and come back here because we do need to work through lunch. I wanted to say one thing while people are walking out. You may or may not believe it but this committee cherishes this time for hearing what you have to say. We understand that we rush you sometimes. We also understand that you don't get a chance to sometimes say all that you want to say. But we do read your material. I know this committee pretty well because I've been on it for awhile. Everyone here cares about doing what's right in trying to help our patients. We want to do the research. We want to get the funding to do the research. We need leadership in that area. Your advocacy for appropriate funding is exactly what we would have hoped for. I just hope that we can meet your expectations of trying to come up with treatments that relieve suffering, ways of preventing the disease using the etiology, and someday not have to have people suffer with a disease that other people think they're just making up.

[Dr. Oleske called a break for lunch.]

Committee Discussion on CDC

Dr. Oleske: In the interest of moving along, recognizing that we have a full agenda this afternoon, I'd like to reconvene us even though we're in the act of eating and try to move the agenda. By the way, Dr. Monroe, I do want to apologize for not making the CDC peer review. I got sick and couldn't get anybody to replace me. I felt very, very bad. It's the worst thing I think that I've ever had as far as my academic career, not being able to go to that meeting. I apologize again.

Dr. Monroe: As Dr. Reeves said, obviously your insights would have been helpful.

Dr. Oleske: I did read everything and sent some comments in. I know that we are anxious for the CDC to continue and possibly make some corrections in course directions so that we can in truth treat CFS with the same vigor that I think we did with AIDS. I think that if we turn that kind attention on this problem, we probably could do something about it. What the CDC did with AIDS was amazing. I think that we would all like to see a reinvigoration of the program so that it starts like it did with AIDS in turning this epidemic around. I love the CDC. I want you guys funded very well.

I'm going to open it up to questions from the group. The only thing I want to say, Bill, is I was interested in your comments about the international community and how much effort will be put into that. While I have no problem with international collaborations, I have to say that I think there are times when the domestic agenda suffers at the behest of an international agenda. I just hope that we don't dilute the concentration on the US. I want to ask you to comment about that.

Dr. Reeves: An excellent comment. Our focus is obviously on the United States. There are three important reasons for international collaboration. One of them I alluded to. There are countries that have put CFS evaluation, diagnosis, and management into their national health systems. The UK is one of those. An international meeting provides the chance to learn from another government that has embraced this illness—perhaps not to the extent that everybody would like—but is trying to work with it as a national health service.

The second reason is that there are studies that you can do because of the type of healthcare. An example is the study that we did of post-infectious fatigue in Australia within a system that could include three quite different agents. We were all very interested in herpes viruses. They used EB and mono as one of those. We were interested in other viruses, for example, West Nile and some of others that might have similar sequella. The same healthcare system could deal with the rickettsial Q fever. People who get ill came into the system and were identified. There was an opportunity to do basic research in a very cost effective manner.

The other reason is that CFS is not just a US problem. There are some extremely good investigators internationally—the Japanese come to mind—that have large multi-faceted programs that we can learn from. The focus is the US, but the real focus is everything that is known about the illness.

Ms. Artman: I want to stay on the international theme. Before this meeting, I sent out a query to those who participated in the CDC stakeholder meeting to find out what they had to say, because I was ill and couldn't attend. Just about everyone came back with comments about either Simon Wesley or Peter White treating this as a purely psychiatric disorder and not as a multi-system complex disorder. There's a perception that in working with the UK, we are adopting that this is a purely psychiatric disorder.

This is a big patient perception issue with the CDC. It's not what you're actually doing; it's what we perceive that you're doing. You need to really place an emphasis on how you want the patient community to view what the CDC is doing.

Japan is doing such remarkable research, I would hope that whatever you do, you pull the Japanese in. I love what they call it: burnout syndrome. Their whole concept is that you do too much and get sick, not as the US tends to think, that we're malingerers. I just want to ask you so it's on the record out there for everyone—what is the CDC's take on this? Do you see it as a purely psychiatric illness?

Dr. Reeves: Of course it is not. One of the very first things that I highlighted out of the stakeholder meeting is that communication has not been optimal. Peter White, the psychiatrist that we work with at Emory, does not look upon CFS as a psychiatric illness. What they are extremely interested in at Emory are the neurologic and brain pathways that mediate this. That is one of the things that Peter White really added to the peer review—he is an expert on autonomic nervous system function. The fact that certain investigators have a reputation in a certain component of the community for thinking that CFS is all in the patient's head is a result of the CDC's problems with communication.

The other problem is that in studies that we've recently published, a large proportion of people who have CFS have serious psychiatric overlays. Those need to be considered as well. But that isn't saying that that is the cause of your illness; that is saying that that is something that needs to be taken care of because it's there with your illness. You cannot ignore it. There is unhappiness with CBT because CBT is "all in your head." Many of you knew me when I was walking on a crutch with a ruptured quadriceps tendon and a year's worth of surgery. A huge part of the rehabilitation therapy was CBT to help me understand what was happening, understand how I could cope, and understand what was expected.

CFS is clearly not a psychiatric illness. It is clearly not just a "brain illness." It is an illness that affects someone's entire body. The brain plays an important part in it, and adaptation of the brain to the various stressors—including an infectious, physical, and emotional stressors—is very, very important. One of the important things that has come out of the research at Emory is that the circuits that appear to be involved in an important group of the patients are those same circuits that are involved in an acute infection. They are the same circuits that are probably important in the reactivation of various herpes viruses. Those mechanisms are what we're looking at. The fact that psychiatrists are involved in no way, shape, or form says it's a psychiatric illness, which it isn't.

Dr. Klimas: A couple of comments for Dr. Miller and Dr. Reeves. You both stressed the importance of communication and your distress over miscommunication in your earlier talks. Communication could be so much better. Were I to develop a clinical trials network and put it through a peer review process, I would never be funded if I didn't have an executive advisory board of experts advising not just the method of the

clinical trial, but what the priority drugs to be tested might be. To do this by contract—to bring academics in through contracts—is not the same thing as having involvement during the design of a protocol, program, and the overall thrust of it.

I would encourage you now, before you start all of this, to really seriously consider how you're going to use the experts out there that are more than willing to lend a hand but really don't want to be given a piece and have you say, "You're a part of our team. Here's your piece" and not have any kind of input into the design or the priorities. That's really important.

Equally, Bill, when you were talking about doing a workshop on management, diagnosis, and evidence-based research, they were in the wrong order. You're doing the evidence-based thing last, which doesn't inform the other two processes. But I don't think that's what you meant to say. I think that it was just that you were rushing through.

The other thing was that *you're* doing it and you'll *involve* the IACFS. That's not what we want. We want a partnership. The IACFS is going forward with management guidelines. They don't want to be members of the CDC process; they want to be full partners. The international community doesn't want to be hand-selected and told, "You're going to help inform the process." They want to be involved as a community, and there are ways to do that.

There are so many fabulous people out there who can help inform the process who have never been tapped and feel, in essence, neglected for their expertise. There's a way to bring people into this and make them feel excited and part it, and you get all that energy for free. Think about all of the great workshops that you've done and what you got out of them for minimal expense. You got a fantastic amount of product out of a very small investment by involving all of those fabulous experts. You can do that all again, but I would just encourage you to go into the development process with partners, not bring them in after the fact or as a consequence of an internal process.

Dr. Reeves: My comment to that would again be kind of complex. Part of it is that communication has not been optimal. The second part concerns the intent of the workshops. You've participated in most of these. The study that we did with you in Gulf War illness is a good example of that. Somebody came to us and said, "This is a neat idea, can we work together to make it better?" All of the workshops that we put together from the beginning were a conscious attempt to identify those people around the world and in this country who were doing serious work, get them together, and ask, "What are the questions? Who should be at the next meeting to work with those questions?" I think we're trying to do that.

But it is also a two-way street. For example, the IACFS/ME has not contacted CDC to say, "We're working on this, would you like to work with us?" It does work both ways. We're working with a variety of people. We go to some; some come to us. When we did the case definition, when we try to get some international consensus on current treatment from a variety of people from a variety of perspectives, we're going to try to

invite everybody that we can. I would hope that other organizations—the IACFS in particular—would be coming to CDC and saying, “We’re doing this and we’d really like you guys involved from the beginning.” There are perceptions kind of the same from both sides of the fence.

Dr. Klimas: I want to make sure that in the end we don’t confuse the world by having two parallel groups that are trying to achieve a very similar goal with nuance and difference in the outcome. That would become a source of conflict and confusion.

Dr. Reeves: That would be absolutely silly. I tried to discuss the timing of meetings in my talk. Those people at the table who do research know about this. When we were doing our big series of meetings, lots of things were coming off at the time; lots of ideas were started. Things right now are just coming off. Things that you are doing, that Lenny is doing, that other people are doing are now coming to fruition. It’s time again to gather at meetings. I think that we’ve been pretty good at trying to do that. I personally think that’s the way that research should be done.

Dr. Snell: I just wanted to commend the CDC for putting together the plan and goals. What I’d like to hear is that there is a real commitment to following through on those goals so that it’s not just an exercise in communication.

Another comment: The presentation that Bill gave was very informative. One thing that I would have liked to have heard is, “This is what happened at the review and this is what we’ve done since.” The peer review took place in November. There are a lot of things that probably could have gotten started. Interfacing with other Federal agencies, I think, is extremely important. We’re here twice a year. We say what we’re going to say. You’re here 365 days a year. Somebody needs to be pushing the CFS agenda from within.

A comment about research: I wasn’t as excited about the breadth of research that has come out of CDC as Bill was. It’s greater than the whole output of the UK. I think that’s a problem. Having all research coming out of one entity provides for a very narrow focus, as capable as the CDC is. I want to start to see that the CDC is producing the smaller amount of research and there’s much more coming out of other entities. Hopefully CDC collaborations with other institutions will enable them to get on the bandwagon.

Lastly, I’d like to comment on the empiric definition that the CDC uses. It seems to be problematic. Bill alluded to it in his talk in terms of people raising issues about it. Given the issues that have been raised, is CDC thinking of going back and looking at that again and seeing whether that is the best what to approach the illness?

Dr. Reeves: I will reiterate what Dr. Oleske said. Everybody in the research program at CDC is committed. They are very talented people and they are committed. The peer review commented about that. CDC as an agency is committed. The particular center that we are in deals with disease ecology. We are in a center that does hard bench

research with modelers and statisticians. It's a center that deals with infectious agents. I think I can speak to this as expertly as anyone given my previous experiences—the agency is behind this and the group doing it is behind it.

The question as to what was done since peer review—that becomes a bit more difficult because when we did the peer review, we thought that we had presented a complete strategic plan. We obviously had not. We had not articulated it properly. We hadn't done diddle with public health. As we began to draft a new strategic plan, it became very difficult. We put it together as a research group and then asked who else is going to look at it? There were some tremendous strategic ideas presented at the stakeholder meeting; things that we would have considered, but we didn't focus.

Creating a new draft strategic plan is one of our accomplishments since the peer review. The review has made everybody in the research group sit back and think in a much more strategic manner. This is not a trivial undertaking. Since the peer review, we've gotten a CSTE fellow. Dr. Boulton is very involved in that particular group. We are increasing our contacts greatly with the health departments in Georgia. That's our kind of model laboratory. We have our first EIS officer. The cowboys that come to CDC to jump on cruise ships or go do Ebola—we were able to present a program that got the attention of that type of person. Those are two things that we've actually done and got onboard. It has galvanized us. We're putting these other meetings together.

In answer to the comment about one entity doing the research—you're completely correct, and what can one do about that? Part of that was the reason for showing the logic model. One can track ISI publications and publications increasing over time. That's people reading other things and starting to do it. People will do research a) if there are funding opportunities and b) if there's other good research being done.

We were astounded with the Duke University exercise. Eight primary publications completely outside of CAMDA (Critical Assessment of Micro array Data Analysis) have come out from, I think, Japan, China, Canada—I forget all of the countries of people who took that data and have used it in ways that we never would have thought of. I would like nothing more than to have ten other programs as big and as productive as ours, either working in the same areas and producing different findings or exploring in different areas. Fostering this also involves communication.

The last subject is the empiric definition. The case definition is problematic for a whole bunch of reasons. The 1994 case definition is the international standard. A lot of effort went into it, but it's a 1994 case definition. It's great, because Dr. Bateman can sit down with a patient, or Dr. Klimas, and talk to them very quickly and apply that. It's quite straightforward. It doesn't require instruments. It's easy. It's also the reason for the heterogeneity in the field. When we had our series of meetings that culminated in 2003, there had been a lot of discussions within the patient community, etc. that this isn't fatigue. "Of course I'm fatigued, but also, I can't think straight. I can't keep my mind on things. I just can't sleep and I don't feel any good when I wake up. Of course I'm fatigued, but that's not my problem."

The 1994 case definition specifies that the fatigue must substantially impair you, nothing else. It's the illness that impairs patients, so we set out to measure the impairment of the illness. And there is a standardized instrument to do it—the SF-36, which has seven scales. They measure impairment and there are population norms. One of our staff, when he was working with a medical school, did a survey of first-year residents in medicine. Eighty percent did not know the difference between “fatigue” and “sleepy”. If Lenny's group in Chicago asks an Hispanic, “Are you fatigued?” and then they ask somebody from the projects, “Are you fatigued?” and they ask somebody else, “Are you fatigued?” or I ask that in Georgia in the rural or metropolitan area, we don't have a clue what the patients think we mean by “fatigued”. The 2003 work group recommended using a standardized instrument to measure dimensions of fatigue so you always will get the same stuff for the same person over time and for different people in different communities and different populations.

Lastly, the committee recommended that there be some sort of standardized instrument to measure the accompanying symptoms, and not just the eight defining ones, but others that might go along with it. That's why we published our symptom inventory. That gives us three reproducible ways of defining people and defining what's wrong with them. And about trying to find a subset of illness? Perhaps a type of mental fatigue that is associated with this kind of gene expression or this kind of autonomic nervous system function or this kind of cognitive dysfunction on testing? I have got a self-report, I can correlate it with hard evidence, and then I can track it over time. So the intent was not to redefine CFS. The intent was to apply reproducible criteria to the three major dimensions of Fukuda.

Will that work in a clinical setting? We may experiment with this in Macon because again, we deal with the clinicians. SF-36 or the MFI Symptom Inventory could be filled out in a doc's office, automatically coded, and when the doc sees the patient, the doc could see the results. Will that work? I don't know. In research studies, you need to have those kinds of inputs. But what might be the optimal clinical diagnosis? That can come out of a workshop. We have the whole question of diagnoses in kids. Are these instruments applicable to them?

We did not attempt to redefine CFS. We attempted to do validated, reproducible criteria exactly as the publication recommended. I think that the download statistics would indicate that a lot of people are accessing that. As many people are accessing that as 67 ISI-cited references from 2003. It is increasingly used and we think it will bring some unity to some part of the research community.

Dr. Snell: It depends whether they're supporting it or whether they're arguing with it.

Dr. Reeves: I think arguing is fine because if somebody does another look at this and says, “Well my data shows this and this and this,” then one can say, “Ok, how did you do that study? What does it really mean? What does what we have mean? How do

they come together? How might we account for that? How might one tweak it?" To me, that's how science works.

Dr. Jason: Let me make three observations and see your reactions.

Certainly Chris and Kim have suggested some issues with the CFS case definition, and you're saying that over time it's going to be used more often, so that's certainly an empirical question as to what happens. The issues I'm going to bring up are a little different.

The CDC at one point suggested that there were about a half million people with this illness, and now they're suggesting there's up to 4 million people. Those prevalence rates have increased tremendously in a very short period of time, a function, we think, of changing from a clinical Fukuda case definition to this empiric case definition. If 2.5 percent of the population has this illness, that means that out of every hundred people, two and a half people have CFS based on this definition. That's interesting, because major depressive disorder has about the same percentage of people. That's kind of interesting, why those two seem to be so close.

You mentioned that the heterogeneity issue was a problem with the Fukuda criteria. The empiric case definition seems to be broader. Even the Wichita data suggested that when both approaches were used with that particular data set. You went from 16 to 45 cases with the different ways of looking at the criteria. Have you reduced heterogeneity by making a broader case definition?

Under SF-36, one subscale of the four has to meet criterion, one of which is "role emotional." Every person who has a major depressive disorder would hit the disability criteria based on role emotional. Does that pose any problem with the empiric case definition?

Lastly, is it possible that some of the concerns that people have is that certain types of non-pharmacological interventions—which you suggested you might be exploring in the future—might have particular positive effects with individuals who have more psychosocial/psychogenic causes for their chronic fatigue? Could that lead to some potential problems for the field? Because as we know, diagnostics is the basis for epidemiology, the basis for treatment studies, the basis for everything we do in the field. There's absolutely nothing as important as the work of diagnostics. Maybe this is beyond this particular question. Maybe we need to have more dialog about case definitions. It is the beginning point and probably the most important point in our field.

Dr. Reeves: If you put the most brilliant paper in the world into a journal and it comes back with archives of terrible comments, either the commenters are trying to get you, or there are other smart people who are thinking of something that you aren't. To me, by definition, when someone is accomplished and has a concern, it's real. It reflects something. It's got to be dealt with.

Our change in prevalence reflects two things. It reflects changes in the field. When we did Wichita, and I think when you did Chicago, how did we get to CFS? We screened the population for fatigue. When someone was fatigued, we worried about CFS. But that may not be what bothered the patient. The patient may be bothered by cognition, and so when you ask him or her if he or she is fatigued, the person answers, “No, I can’t think straight. I can’t sleep. I hurt all over.”

In the Georgia study, this became clear. We screened the population not for fatigue; we screened the population for unwellness. We had criteria. They were basically problems with thinking, sleeping, hurting, and fatigue. If someone replied positively to that, we gave them the more detailed questionnaire. About 20-30 percent of people who did not endorse fatigue as their primary symptom met criteria on the screening for CFS. We cast a broader net, then we applied the Fukuda criteria on the telephone. Again, 20-30 percent of people who did not complain about fatigue endorsed the Fukuda criteria.

Our screening was quite different; we cast a broader net—that is as important a reason why the number of CFS patients went up as anything. We actually captured people that we missed in Wichita and that you probably missed in Chicago—unwell people who in fact have CFS, but their major problem isn’t fatigue.

We give a psychiatric evaluation for major depressive disorders. This is important in the research. The 2003 work group recommended using one of two tests. One is the psychiatric screening instrument endorsed by neuro health organizations and the other has to be administered by trained psychiatric social workers—the research standard for diagnosis of Axis I disorders. When we diagnose the 20 percent of patients who have major depressive disorders, we say, “You have CFS *and* you have a major depressive disorder.”

We had great angst about this in the 1994 case definition. There were several meetings that talked about it. I don’t remember who from here attended. Major depressive disorder should not be considered exclusionary. For the purpose of research studies, melancholic depression is exclusionary as are bipolar disorders. It was decided that if you have major depressive disorder, it must be identified, and then it’s a stratification variable. 4.5 percent meet the criteria with the mandatory exclusions out.

The 2003 work group did not recommend scales, so we selected the scales that we selected because we felt that they best represented the type of disability or the type of fatigue. Major depressive disorder on the role emotional is an important one, but that’s also an important source of disability in people who don’t have major depressive disorders, so those without CFS and without a major depressive disorder may be low in that as well.

Dr. Oleske remarked upon the length and complexity of CFSAC member’s questions. **Dr. Reeves** suggested that members could email additional thoughts or invite him to join subcommittee conference calls.

Dr. Jones responded to that suggestion: Just to clarify, the role of the subcommittees is primarily to prepare for the meetings. When we do anything formally in dialog about specific issues, we have to be very careful, because the public has the right to participate in that dialog. With all due respect, our subcommittees are created and exist within the current Advisory Committee Act requirements with a specific purpose. I would hate to put the committee or the subcommittees in jeopardy. If we need further dialog on the issues that we're discussing with Dr. Reeves, we can have a special public session, if need be.

CDC has invited comment. Let me clarify that as well. Bill, Mike, or Steve, I don't know if you want to make that specific declarative statement for the record here. I think it would be important to clarify. If I understand you process correctly, the public can still comment directly to the CDC on your five-year strategic plan. That comment need not occur solely through CFSAC.

Dr. Miller: You can comment either through the CDC CFS website or through the HHS website. This plan is still in draft form. That's why we're discussing this today. Our definition of communication is two-way communication. If it goes just one way, it's just information, and that's not very helpful very often. That's why we're in this business now of being a lot more transparent and really inviting further comments. We welcome that.

Dr. Cavaille-Coll: One thing that people need to know is that if we change the definition of and the criteria for the diagnosis of CFS, it's going to really affect tremendously the ability of pharmaceutical companies to do clinical trials in CFS. That's one thing.

The other thing is that SF-36, I believe, is still a proprietary product and people do have to pay to use it. I think that we need to be very mindful as to what we're doing and the impact that it will have on the ability to do clinical trials in CFS.

Dr. Reeves: Two factual things on that. The case definition has not in any way, shape, or form been changed. Secondly, you are correct about the SF-36. We use it because we licensed it. There is a non-proprietary version from the Rand Corporation that is in public domain.

Dr. Hartz: My impression about Federal agencies is that they are primarily designed to stimulate research and assist in research. My impression about the CDC is that in research on CFS, it is a fatigue czar or at the minimum, a PI-type setting where it's very much internal, not designed to help other people. You brought up an example where that's not the case. I would like to know more about how you see the role of the CDC. If you see it as a way of supporting and stimulating research in others, what sorts of things do you plan to do to help others with their research?

Dr. Monroe: Historically, CDC has often been the source of the single world expert—

or one of the world experts—on a certain bug. I come from infectious disease where we were all focused on our own pet bug. Often it was only one or two people deep, but we were very much the authority on that bug. CFS is a complicated beast, so the approach has been to have a multi-faceted team that has psychiatrists, statisticians, array people—all kinds of people focusing on the same problem. One of the things that this does is make the program bigger than a lot of the other programs in which just one or two people focus on a single bug. That's why we need to have a large intramural program to work on this.

In terms of what CDC can do for the field, we're not primarily a grant agency, so we don't support R01-type research grants. What we can do is take on the things that other people can't, such as these large population-based studies. They are expensive and take a long time to show fruition. They are difficult to do as part of an R01-supported research program where you need results in order to get the next grant. I think that we can serve as a sounding board and a resource for the research community, but I don't think that CDC's role is to "support" by providing grants to academic researchers.

Dr. Hartz: In addition to partnering, having conferences, listening, and interacting with other people, sharing data is a way to give others a chance to influence your results. My experience has been that CDC is interested in subcontractors rather than partners. I'm not sure what the expertise is at CDC. Maybe you have all the expertise that you need, but I would doubt that because as you mentioned, CFS is a complex disease. I would imagine that you could benefit from greater interactions with the academic community. I wasn't sure what you were doing to enhance this.

Dr. Oleske: I somewhat disagree with that because I've had my experiences with CDC. For example, I think that the CDC at times has supported extramural research. My original grant was from the CDC. I think that the CDC has always been a leader in bringing in people and partnering with them and not having limited partnerships but rather, full and true partnerships. That's been my experience.

I'll have to say, though, with CFS it's not as true. I think the CDC does have lots of expertise now in CFS but...I'm not trying to start a fight, believe me. I really love the CDC. I was down there for two years when I was at Emory. I've worked there. I was the first person to do a CD4 count at CDC a long, long time ago. But for some reason, with CFS, it does seem that you'd rather have a paternalistic relationship with us investigators. I think that's important. I think what you're hearing is that this group is trying to get the CDC to be what the CDC has always been. This paternalism is so out of character. I think that's what you're hearing from the panel. We just want to have an open partnership with the CDC.

I think that it's appropriate for you to be involved in supporting a network if you want to do that. You've done it in other areas. But it seems like CFS is treated differently than almost anything else I've seen at the CDC, and I've been around awhile. You guys do have my utmost respect. But you're hearing from most of the people on the panel that

we feel that there is an exclusion of a full partnership, and that's not how the CDC usually works. I don't think it's good for you to do it in this particular disease because our patients are very knowledgeable about their condition. I don't think they want to be treated paternalistically. They want us, their doctors, to have full partnership with you and they want to have a partnership too. Please understand that this is meant to improve what is going on, not to tear it down.

Dr. Glaser: That was a very good statement. Bill, some science. Do you think that EBV or HSV6 have anything to do with CFS?

Dr. Reeves: I think that there is a subset of people with CFS for which an acute infection—be it herpes, Q fever, Ross River, Lyme disease, dengue—is what sets it off. It is not all of the cases. That's been part of the problem with research, because it is heterogeneous. For example, most of providers' patients got sick all at once. They got mono and never got better. That's what set CFS off. We know that 10 percent of people with those acute infections don't get better. We do know that 75 percent of people in the community slowly got CFS. A virus probably didn't set that off.

The question of latent viruses—herpes group viruses, in particular HHV6—is open to look at. Can reactivation of HHV6 be involved if the pathophysiology causing CFS was turned on when CFS is bad? Yes, it certainly can. What proportion of the community is that? What proportion might be made better by appropriate therapy? I don't know. But what I *do* know is that the study design for getting at that is extremely complex, particularly complex in the case of latent viruses like HHV6.

Dr. Glaser: In your overview, I think some of us would have liked to have seen examples of some of the kinds of studies that you plan on doing over the next two or three years to get at that issue. You and I have agreed that probably the two most important things that the field needs to have dealt with, finally, after 20 years, are etiology and biomarkers. So you would have thought that that would have been right at the top of your list in terms of your plans. Where are you on that? Give us some examples of some studies that you have planned.

Dr. Reeves: I don't have an easy answer for you.

Dr. Glaser: Yeah, there isn't an easy answer.

Dr. Reeves: One of the reasons that I presented—we've been talking about partnerships. We've been talking about funding. When I first came to CDC, I was very interested in doing EBV and mononucleosis and my mentor said, "Don't do that. There are a ton of really good academicians who are doing that. Help them with some public health aspects of it, but there's no reason for you to replicate their programs."

There are some extremely talented people doing HHV6—basic investigators, laboratorians. I don't have the funds to do it. Given the platform that I have and given what I *can* do, which are equally important priorities, I would certainly be ecstatic. I had

some of these ideas in working on the strategic plan. Jose Montoya, an investigator, came to us in his original studies and said, "I'd like you to help me with my instrumentation." We did a lot of work with him on his instrumentation, including helping him with analysis and replicating some of his analysis.

We're working on mechanisms of reactivation. I don't have the resources to begin a whole HHV6 program. If people were to say, "Gosh, we really want to collaborate with CDC. How might your expertise and our expertise go together on HHV6?"—it's a win-win.

I don't look upon collaboration as giving a contract or giving somebody money. I look upon it as a situation in which we've both got our resources and interests. How can we focus on this one thing that we can both make work?

Dr. Glaser: So your response is that the reason why it's not there is that you don't have the resources to deal with that area of research?

Dr. Reeves: That's correct, and other people do. We could work together so that nobody would have to waste resources.

Dr. Cavaille-Coll: I've been part of the coordinating committee for many, many, many years and I do remember an eloquent presentation by Steve Strauss in which he presented all the different types of work that he had done with different types of viruses. I do agree that they may be the techniques of change, since he has died and there probably are new ways of looking at this. But at the time that the products for CFS were transferred from the Center for Biologics and Evaluation to the Division of Anti-Viral Drug Products, he did provide us with a very comprehensive white paper that explained how this was not a viral illness. He's also presented, in the previous existences of this committee, some very eloquent research about this.

So I agree that maybe the techniques now for evaluating virological diseases have changed and there's probably still room for doing work there, but I think that we do need to remember the work that he did. One of the things that happened when we went from a coordinating committee to an advisory committee is that on the website for the coordinating committee, all the minutes and all the presentations that had been presented to us have disappeared. But I want people to remember that this is not new. On the other hand, I do believe that maybe with new technologies that have been developed since he died, there's still room for evaluation. But we should not forget the past.

Ms. Artman: Given budget constraints, I think the number one priority we need to look at is biomarkers. That is going to impact patients more than anything else. I would love to see the CDC do another meeting like they did, open up their data, invite people in and tell them, "We're looking for a biomarker. " I asked the committee casually this morning at breakfast, is there a way that we can do a cash prize? Whoever finds the biomarker that's testable, we give them a million bucks. That's going to impact every

patient. That's going to impact every researcher. So, I think that's the number one priority—a biomarker. If you drop just about everything else and do a biomarker, we'd be griping, but if you found a biomarker, we'd all be thrilled.

The second thing is, Kim asked about budget. Patients have brought this up—we need to demand a hundred million dollars. The branch of government that we officially work for has no control over money. Congress does. I can't give you a hundred million dollars. However, I can say for the record to any patient who wants to go to Capitol Hill or write to a Congressman that the amount in the budget that we see going to NIH and CDC for CFS research is embarrassing. When I think that I have psoriasis, and psoriasis gets more money than the illness that disables me, it is offensive. I'm saying this to you because I think CDC should have more money; I think NIH should have more money. If I had the magic checkbook, I would put pull it out and write you checks. I would love to see more people involved in letting the world know that we need more money for research for this illness. Why? Because it is such a big deal. It does affect so many people.

I do have one question for Bill. When you're doing the Georgia study, when you're looking at the CFS group of patients, do they match the Wichita group in case definition and subgroup? Are you finding the same subsets in matching both groups? Are you able to actually compare group to group?

Dr. Reeves: That will come out of the GCRC study. I want to make one quick comment on biomarkers. If it was easy, we would have one. Looking for biomarkers is not trivial because the subsets are different. That's why you require a population to look at the clinical course. What about those who are getting better? Research on biomarkers includes looking at clinical markers and many other things. You can't just grab a population and do biomarkers. It has a big lag period and it is much more complex now. What is all the stuff going on in the people's brains and bodies and autonomic nervous systems that we're trying to put together? There is a chunk of field work that has to happen before you can get that. All that field stuff has to be there in order to have the groups in which you can look for biomarkers.

Dr. Klimas: Can you achieve the goals of your strategic plan as you've laid it out with \$1.9 million a year?

Dr. Reeves: We don't have a choice. That's our budget.

Dr. Klimas: That's not the question. Can you achieve it with that budget?

Dr. Reeves: I don't know.

Dr. Klimas: I'm concerned because you've put out a lot of things that need to be done. There's an \$8 million budget up there. The clinical trials are four or five million dollars.

Dr. Reeves: I can't answer that. Right now, we can do what we're doing with the budget that we have now. Can we get back to where we were when we had a very multi-faceted program with that budget? No. It's impossible. We cannot go back and do that. We can achieve what we're trying to achieve in the plan with the current budget, but it won't happen fast, budget or no budget.

Dr. Monroe: It wouldn't be a good plan if there wasn't a stretch to begin with and that's why I think it's critical that in two years, we look at what progress we have made against the goals. We can determine which are the most fruitful avenues and make adjustments. The yes-no answer is no. We cannot achieve everything that is in the plan with the current budget.

Dr. Klimas: Moving it up a notch, if more money is needed, is there any money to be had?

Dr. Reeves: Once again, it's not a plea for money. I'm trying to lay that out as a reality. There are important "if's": *if* some of the pharmaceutical companies become very interested; *if* the GCRC study shows what we think it might show. Part of the problem with the strategic plan is that I don't know what the findings are going to be six months or a year from now.

Dr. Miller: What Congress appropriates is set by Congress. We, of course, will take what they appropriate to us. The problem is, if that appropriation stays level, then in the long run, the value of that funding goes down. But what if in today's economy, there are going to be cuts across the board? That could also impact our ability to achieve the goals that we'd like to achieve. We'd like to say that yes, we can accomplish it, but it is a stretch, in the hopes that our appropriations would increase. Advocacy for those funds would go a long way for both NIH and for CDC.

Dr. Oleske: I'm hearing cuts, but I'm also hearing \$30 billion for healthcare in the President's initiative. If the CDC's not getting a piece of that, I don't understand. There are cuts in lots of areas, but it didn't seem like healthcare was one of them.

Dr. Miller: I don't know what the details are of what the CDC will eventually end up with or what portion of that money will already be earmarked for one thing or another. There are no decreases at this point in CFS funding at CDC, but the funding is essentially level. There are no increases that we're aware of at this point.

Dr. Bateman: My question was pretty much like Nancy's. My main concern is that although these goals are very promising and they are so needed, it just seems impossible that the current budget or even the projected budget would come close. This is especially true for Goal 2 and Goal 3, which are about diagnosis and management and implementing clinical trials and treatment. Those are so critical. What I worry about is that we give voice to these goals but they can't be supported with the funding. What does that do for our timeline of trying to make progress? To what

extent can the budget support these goals and what portion of these goals will be supported?

Dr. Reeves: We need to address that in the next iteration.

Dr. Bateman: What is the timeline for the implementation of this five-year plan?

Dr. Reeves: Hopefully dates are in there. I have prepared a GANT chart. It's not in my presentation because it would be terribly complex. We're looking at data ourselves. I think the thing to do would be to read it, think about it, give us comments, and I can address that more specifically.

Dr. Miller: I think that my goal in terms of intervention is that we get to a point sometime during the five-year plan where we're ready with the defined study population, we implement some intervention that shows promise, and we're to measure the impact of that intervention.

Dr. Reeves: We talked about a collaboration with Mayo on a CBT/GEEM intervention. That's two years out, maybe more. Attacking why people are not utilizing healthcare may be different. When we look at our baseline population study, 50 percent of the people have seen a doctor for their CFS, half haven't. Lenny found the same thing in his study. We found the same thing in Wichita. We've measured the barriers to utilization. We can try to attack those barriers through education. That doesn't cost a lot. That can be done with media that CDC can get in that area. I can measure the change the next time I do a follow up. I can put in that kind of intervention on the population basis. What do docs need to know about this? What can I do intensively in the physician population of Macon that does not cost me another million dollars? I already know what they say they need to know. I know what they don't know. I know what they're doing with patients that can be modified and measured.

Intervention is not just trials. There is also population intervention for both the patients and the providers. The state health department and the local health department, which has this as a major problem, is going to be very interested in collaborating on piloting this kind of intervention. Intervention is really not quite as simple as just a trial. It involves other things that this committee is interested in, like KAB and access and utilization of healthcare.

Dr. Oleske: Steve, what I think you were trying to say can be expressed by my favorite quote: "Ah, but a man's reach should exceed his grasp, or what's a heaven for?" That's a good attitude.

Mr. Newfield: I know you said you weren't making a plea for money, so I'm going to throw the money ball up to let you spike it. How much money do you need and what would you use it for. We can give recommendations that have flesh to them to hopefully support your efforts. If we talk one, two, or three years out, how much money do you need and what would you use it for?

Dr. Hanna: I just want to make a clarification, because the issue of NIH funding has come up several times. We are not funded by Congress for CFS as the CDC is. We have no allocation for CFS. Any budget figures that you see are based purely on grants that come in, are accepted, and funded. Each year the budget dollars are based on the projection from those. There are no salaries paid to any NIH personnel, including me. Everything that we do is paid by the institutes and by the ORWH. The only budget you see at NIH represents research dollars.

Dr. Miller: I think that might be something to think about for a recommendation. Jason, if you would like a specific answer regarding how much we need and what we would do with it, give us time to really think about that and we'd be glad to offer something to the committee.

Dr. Snell: Presumably when you operationalize your five-year plan, you'll put a budget together for it.

Dr. Miller: Those kinds of discussions are usually framed in the form of a professional judgment document where we're asked to speculate wildly about what one would do with numbers. In this setting, we're dealing with the appropriated amounts that we have as requested by the President and authorized by Congress.

Dr. Jason: The external peer review indicated that there would be a recommendation for a two-year follow up. I was wondering if you could comment upon having some type of continuing review of the progress of this five-year plan.

Also—you've talked about Peter White in several contexts. Is he one of the people who are being involved in some of the collaborations that you're doing?

And the final thing, I read a letter in our package that I thought was extremely interesting. I want to read a couple of sentences of it and get your comments on it. I don't know this person. He says, "My name is Reverend Allyson K. Day and I am completely disabled with CFS and FM. Although the CDC is located in Atlanta and the renowned Emory teaching hospital is located here, not one doctor will test or treat CFS. There was no doctor that would see me for either issue. While I was a patient at the large city hospital for indigent care, the doctors, trained at Emory, were taught nothing about CFS or FM." I recognize that this is one person, but I'm wondering if you could comment on that and also if you could tell us why you think there are lots of people out in the field who, particularly in the patient community, have mixed feelings about some of the work that occurs at your laboratory.

Dr. Miller: I don't think that's a yes/no question, but we'll try to be brief.

Dr. Reeves: That's an impossible question to answer, particularly in a public meeting. I can tell you, however, that the Emory School of Medicine does not actively teach

against FM or any of the other things. That's one person's opinion for whatever reason that person came to that conclusion.

As far as the strategic plan, our plan right now is to formally reevaluate it in two years.

The collaboration with Peter White is largely because Peter White came to us when the national health service in the UK was trying to design its program and formulate recommendations about what the health service in the UK should do. We've consulted with them as far as our ideas and our expertise, and we collaborate with Dr. White on the PACE trial. He's an unusually intelligent individual—you've read some of his comments on some of our articles—whom we enjoy sparring with. He is an expert on autonomic nervous system function and he's highly instrumental in all of the hurdles, both with patients with the government and with physicians, in trying to put together, given the current state of knowledge, a national program.

CFSAC members decided to adjourn for 10 minutes to conduct a portion of the subcommittee meetings that were delayed in order to accommodate a dialog with Dr. Reeves.

Dr. Jones requested that CFSAC members approve the minutes of the November 2008 meeting before adjourning.

CFSAC members unanimously approved the minutes from their November 2008 meeting.

[Dr. Oleske adjourned the CFSAC meeting so that subcommittees could gather for ten minutes to finalize their reports.]

Subcommittee Reports

Research Subcommittee

Dr. Jason, subcommittee chair, presented the report:

We have had meetings every month to two months since the last meeting. We certainly have considered a number of issues that I want to review briefly:

- The Center for Scientific Review and NIH (and CDC) support for grants.
- The CDC's five-year plan.

CSR Issues

- **Tomorrow Dr. [Cheryl] Kitt [CSR Deputy Director] is going to be meeting with our subcommittee for lunch.** We hope to continue meeting with her

concerning the issue of the CFS SEP (Special Emphasis Panel). As you probably know, the SEP is a critical vehicle for the support of CFS research grants in the Federal government (one of the past SROs (Scientific Review Officers) is in the audience). Right now there is a temporary person who's in charge of that review committee, and that temporary person has a tremendous amount of discretion in terms of the selection of reviewers. The issue of how grants are reviewed is certainly something about which we've had some preliminary discussions with Dr. Kitt.

- **Ron [Dr. Glaser] has done a fascinating analysis** where he looked at the expertise of reviewers on the CFS SEP and found that approximately 15% had published an article in the CFS area. We want to continue to think about ways that we can get more people with knowledge of CFS on the review committee that evaluates most of the grants in this area. We'll continue some of those discussions. I must say that Dr. Kitt has been extremely generous with her time. We work closely in association with Eleanor (Hanna) as we think about how to get more grants submitted, more grants evaluated, and hopefully more grants funded. That's certainly the mission.
- We appreciate the fact that at the **IACFS/ME meeting**, there was a workshop on grants that was well attended. There was a tremendous amount of interest of people at that meeting in developing grant proposals, particularly during this very exciting time of the stimulus plan.

CDC Five-Year Plan

- We had quite a few discussions about the five-year plan and I think that our general sense was that **we didn't have a lot of information prior to the meeting at the CDC**. The information that was provided by the CDC was somewhat sketchy. Their response to that was they were looking for input, and certainly we can understand that they wanted to get input from the professional and the patient community.

We have now been provided with the plan. I don't think that any of our members have had a chance to read it because it was just provided to us before this meeting. There's some feeling among the subcommittee members that if we can get this material in advance, we can better digest the information and react to it. Certainly I will schedule another meeting of the research subcommittee so that we can really talk about the five-year plan.

- **One of our recommendations** is very similar to the recommendations of the external peer review:

We concur with the CDC CFS research program's external peer review's recommendations that a progress report that refers to the five-year written

plan be reviewed by an external panel two years following the November 2008 meeting of the external review group.

That is one motion that we would like to put on the floor. We certainly think that the response of the CDC representatives was pretty positive to that. In fact, we're hoping that there's much more dialog and a regular ongoing set of communications with our Research Subcommittee so that we can continue to hear what they're thinking of doing and what they can and can't do with available resources. That's something that would help us think through where the priorities are. We can then have more strategic input for those plans.

- In addition, we have an old recommendation. We don't need to vote on this, but to remind everyone, the November 2007 CFSAC recommended that an extramural effort on CFS be directed by the Office of the Director of the CDC. That's a recommendation that has been voted on in the past by this group. There have been several discussions about that issue in the past.

The CDC has many cooperative agreements, contracts, and grants that they supply to investigators. I think that there's a sense that there could be strategic issues at the CDC in the area of CFS that the agency might want to consider. Just in our brief discussion here, we talked about quite a few issues involving methods, assessment, diagnosis—all these basic parameters that have a lot to do with how the CDC measures CFS and understands it.

- Although we didn't take a vote, I think that many of our members agree with the external peer review group that there is an absence of research linkages to other public health institutions. We appreciate the fact that the CDC is going to be working on this issue. We'll see how that's rectified. The external peer review group felt that the CDC was ideally placed to organize detailed planning of international CFS research networks. We think that's very important to do. The key question is, now that they've been put on the record, will those types of things occur?

One of our members—Art Hartz—had to go back to the hotel. But I do have Ron here and our *ex officio* members, and I want to give them a chance to comment as well.

SEP/Congressional Funding

Dr. Glaser: You've heard this discussion again about the importance of determining the etiology and a biomarker or biomarkers for CFS. For 20 years we've had a mystery: What causes CFS? And we still have a mystery. This is very complex stuff and quite frankly, we're not so smart. We have a lot to learn about a lot of things that cause diseases and how the diseases evolve. Part of the problem, as Len pointed out, was the dissatisfaction with the SEP in terms of the review process. Part of the spin off of that interaction is that eventually, when investigators try to get a grant funded on CFS and get rejected time after time, they're going to get discouraged. Word of mouth gets

around. People say, “Why bother submitting a proposal if the likelihood of getting it funded isn’t very good?”

In the grant data that was handed out today, if you include only CFS-related tables, only three of the grants funded are on biomarkers and two are on etiology. There’s no way that we’re going to solve the mystery of what causes CFS with those kinds of numbers. That bothers me a lot. Hopefully we can get Cheryl Kitt to deal with the issue of that SEP. I think that she’s always been receptive to the possibility of making this more multidisciplinary in nature, because it needs to be multidisciplinary in nature. That’s one thing that we’re going to try to do. As Eleanor pointed out, Congress hasn’t mandated any money for CFS. We have to deal with that and we have to deal with the review process so that it attracts people back to make an investment of their time to work in this important area.

Federal CFS Research Priorities

Dr. Jason: Michael brought up an interesting issue that our Research Subcommittee could be doing. We can prioritize research areas, then see which have more work going on and which have less. We think that’s a reasonable task for us to be thinking about.

Dr. Miller: The purpose of bringing it up was that I’m not sure that this advisory committee’s views on an official research agenda are documented. These views would not get down to the level of PIs or what’s going on in any one person’s laboratory. The views would express what this committee agrees are the major research gaps that stand out for CFS and the priority in which how those gaps should be addressed. That way, when we go to the Secretary with recommendations, the Secretary would be very clear on what this committee considers important research agendas and research areas.

Dr. Jason: We are particularly appreciative of Pat Fero and the tremendous amount of work that she has done to organize information in terms of the amount of grant support at NIH. That has been helpful to our subcommittee.

No Response to CFSAC Recommendations

I wanted to bring up one other issue that happened in our subcommittee. I think that it’s important that members of this committee be apprised that at one point we had been talking about past CFSAC recommendations and Wanda said that most of our recommendations over the past five years had not been delivered to the HHS Secretary.

Dr. Jones: No, they went to the Secretary. They were transmitted. They have not been responded to by the Secretary.

Dr. Jason: I think you suggested that it might have happened with other advisory committees. That's something that I would like to put on the agenda. You are a person who has brought a tremendous amount of organization to this committee—not just the web cast, but all the support. We are not trying to put fingers on anybody to blame. But if we have a systemic problem that recommendations are going to the Secretary and they're not being acted upon, I think that's an issue that we should be thinking about.

Dr. Jones: I think you raise a valid point. The one thing that nobody's staffing and that the advisory committee has no control over is what happens once we do our duty of transmitting those recommendations to the Secretary or to whomever the advisory committee is supposed to be providing its advice. I do know that the *ex officio* agencies do take the recommendations. You can see little bits of progress that have been made because the *ex officios* come to these meetings and they listen. There may be things that they simply can't share back yet. Things take time.

From my point of view, if the Secretary has an advisory committee tasked to provide advice on a particular subject matter and that committee takes the time and taxpayer resources to provide that expert commentary and advice, the very least the Secretary's staff can do is acknowledge and thank the committee for its work and ensure that in turn, these are being transmitted to the responsible agencies.

I can tell you from my almost 12 years in Washington, I have not been retiring and shy and quiet, but I am an organization person. I understand and respect what has to be done by HHS to uphold its fiduciary and other responsibilities. What you have with our office now tasked to staff this committee is not just one person working part time and tending things as she can. You've got a very strong voice in an office with a good reputation in the department and within the Office of Public Health and Science and an Assistant Secretary of Health that we hope will be confirmed soon who is a good public health person. I've already made him aware of the committee's existence. Beyond that I couldn't say much. I will not be shy and retiring about making sure that not only do these recommendations get transmitted, but that they get more than just a "nice report" and filed on a shelf.

By that same perspective, I think it behooves every advisory committee to understand that just generating endless task lists with 50 items that you want done is not going to be reasonable for anybody. If you can prioritize—name the top two or three or five actionable and reasonable items; the briefer the better—then we might see progress between now and the next meeting. And then the next meeting will generate additional recommendations, and the meeting after that, and the meeting after that.

Advisory committees are intended to be somewhat iterative processes, if you will, because work moves on. Agency appropriations evolve; the science evolves. The frustration comes when you feel like you've been on a treadmill. If you look back through past recommendations that CFSAC has generated, there's some resonance. There are some very similar things. It doesn't mean that nothing is being done. But perhaps we've missed some opportunities that we should try to seize differently. My

office remains committed to helping this committee achieve that as we do the transmittals to the Secretary and follow through on the work done by the advisory committee.

Dr. Jason: What I would suggest is that if we're going to go back and look at some of those past recommendations and see what's happened, that's certainly a critical issue. Some of them might no longer be appropriate. I would say that going forward, at least with what's current in terms of this CDC five-year plan, I would hope that if we're going to have a couple of targeted recommendations, that one of them probably should involve some of the issues that we've been discussing this morning.

Dr. Jones: My role is simply to facilitate that process. You are the advisory committee; I would leave recommendations to you. I will do everything in my power to make sure those get forwarded and are not just a "nice report."

Patient Care/Quality of Life Subcommittee

Ms. Artman, subcommittee chair, presented the report:

Pediatric CFS and Education

We have had several conference calls since the last meeting and several emails back and forth. We're very, very excited about tomorrow's pediatric and education meeting. We are hoping that the Department of Education, David Bell, and those who are participating in this meeting tomorrow will leave with an ability to create a game plan to make the lives of every parent and every child with the illness much easier to deal with. We've been asking Education to come since our very first CFSAC meeting and they're coming. Applauds to Wanda for getting this done.

Web Cast

Since our committee has been started, and I know years before we started pestering Anand, we've been asking for a means for taking this to the public. I know a lot of patient groups—applauds to all of you and every individual who has asked for this. Thank you to the NIH and HHS for broadcasting and making this available. This is a fantastic venue for every patient who's stuck at home, validation that their illness is real, and information that the people on this committee care about them. They may be frustrated with us. Fine. But we care about them and we want to see something done about this illness.

SSA

We have completely tabled what we have done for the last three months. We wanted to discuss ADA (Americans with Disabilities Act) and employment. There's something else that's been going on that we have a problem with and we want to address it,

specifically at the next meeting. For years we've been asking Dr. Desi for information, and it all goes up the ladder.

We would like to formally request here and now that someone from management from SSA be able to come to the next meeting. Our subcommittee is going to come up with a list of questions that we have specifically to be answered so that you have some hard data for management to come back to us with. There are a lot of questions that keep getting left unanswered. We want to go up the food chain or pay grade or however it's formally said because there are some very specific issues.

Access to Care

Something else that we are concerned with is access to care. It's something that we hear over and over and over again. I'm sure that everyone on the committee reads all of the written testimony. I was telling someone earlier, it's heartbreaking to read it because it's very personal. I've experienced a lot of it. When you've experienced it, it's even worse, because it brings it all back.

It's unbelievable to read that someone in Houston, TX, with CFS can't find a physician. Houston, for those of you who have never there, is not only a huge city, it's a huge medical city. They have specialists there for diseases that nobody's ever heard of except the people who have it. That's Houston. And for those people to not be able to have a CFS doctor...I was in "Podunk" Middleburg, FL, which is boonie Florida. No one's ever heard of it. I had a CFS doctor that I could go to. I train the doctors around me. I give them toolkits. I tell people that I have chronic fatigue syndrome— and that's muscle fatigue, that's not tired fatigue. I explain the illness to them and they're responsive to that. It's so important for patients to have access to care.

We want to tackle SSA and get our questions answered. But we really want to look at what we can do to fix the problem. We don't want to just talk the talk. We want to find a solution. How do we bring new practitioners to the field, be they physical therapists, nurse practitioners, or massage therapists? I don't care what your discipline is, we need people who are educated enough to be able to do something to benefit the patient community, who are suffering with pain and all the things that this complex syndrome deals with. That includes addiction issues. I heard recently of someone who has an alcohol issue who can't get into rehab because they are dealing with FM pain. It's a cross-over.

How do we deal with this stuff? These are things that get glossed over, but there are some nitty gritty things we'd like to look at. That's what we're going to be moving forward with. Anyone in the patient community who wants to contact us and give us input and feedback, those are the issues that we're going to be looking at. And if you see something we are not covering that you think falls under the domain of our committee, we want to know. I want these doctors not to have to work on our illness anymore. I want a solution. If you're brilliant and have an idea, contact us.

Education Subcommittee

Ms. Healy, subcommittee chair, presented the report:

Pediatric CFS and Education

Our Education Subcommittee met several times via conference call and spent most of our time on continuing the theme of last fall's meeting when Dr. Rowe talked to us about pediatric CFS. We wanted to use that as a foundation to bring forward some of the programs that are suggested for tomorrow. Dr. Bateman can talk about the planning that she put into the inviting of folks who she knows in Utah. A panel of young people put together a DVD, which we hope will be an innovative way to present the perspective of young people having this disease.

Provider Education

With the theme of education, we are very pleased to see that the CDC's five-year plan has as its second goal to improve clinical management providing evidence-based education materials addressing the evaluation and clinical management of CFS. That's been the whole crux of our issue, and we've heard this over and over, reiterated throughout the testimony today, in the past, and likely in the future. When so many patients go undiagnosed and/or have limited access to care, they may get a diagnosis, but not effective treatment.

We know that provider education is still necessary. There have been efforts in the past that we've taken to calling CFS 101, but now we have to go to CFS at the 400 and 500 and upper graduate levels. That's part of what our committee will continue to work on. We will try to come up with some specific recommendations that can perhaps improve the focus of the programs at CDC, HRSA, and others so that the programs are effective.

Dr. Klimas: I'd love to get some feedback from Wanda and other members of the committee because we're trying to frame the next step in the right language. I don't want to get hung up on the micromanaging or the minutiae of the recommendation. I would like to be a little grandiose, but have it achievable.

The grandiose thing would be to prepare a challenge grant format to deliver a model care system for a complex illness such as CFS, which has the extraordinary statistic of less than 50 percent of the people seeing a physician and 85 percent going undiagnosed. And then the next extraordinary piece of data is that the 15 percent that do come to care and are diagnosed have very limited access to knowledgeable care. I'd like to hope that our committee could put together a resolution that would be seen seriously as an opportunity.

It's exciting to be in a new Administration. It's exciting to be in your office with the enthusiasm of your staff. We come to this not so much to replay an old resolution, though that resolution is there over and over and over again that there needs to be

centers of excellence that could try to develop healthcare and research. We would like to instead reframe and reformat our recommendation in a way that says, "Step up and do something."

I said, and I think I'm right in this, that CFS is the most broken illness there is that I know of in the healthcare system in terms of being misunderstood and misrepresented and having lack of access and poor standards of care. Everything about CFS is a challenge. If we step up to this challenge, we can fix the whole thing. And I don't mean CFS; I mean the whole healthcare system. I think there's an opportunity here, and I'd like to frame it in a way that the new Secretary would think, "Oh, cool. I think this is a good idea." I would like people to ruminate on that overnight. Tomorrow, when we come back to our working subcommittees, feel free to break ranks with your panel and come to our subcommittee to help put this thing together. Let's see if we can't do it in a nice bullet format that sounds like it might be read and understood, but also seized.

Dr. Oleske: I found in September '04 the first recommendation with centers of excellence. The next year, that was still number one. So that goes back a long ways. I know that when Ken Friedman was on the committee, he talked a lot about the importance of introducing the topic of CFS in medical schools, and by having scholarships, he single handedly has done that in New Jersey. We have a specific medical student scholar in CFS who has advocated an understanding of that disease and, if you will, spread the word that there is such a disease.

We planted it deliberately into our educational program on humanism in medicine, which is a very popular theme right now in medical schools, and so we have buy-in at our university and CFS is introduced in the first year. I wasn't sure it was going to work, but seeing it develop, I think Ken was right. I think he sat on the CFSAC Education Subcommittee, and he used to push that at every one of the meetings. He's not here now and so I'm not necessarily speaking for him, but I do think that if there is a way, we should encourage medical schools to recognize the legitimacy of CFS. Sometimes you can make it remembered because there's a medical student walking around who is given a scholarship for CFS. I just want to bring that up because it was a big part of what Ken did and I think he would be mad if I didn't.

Ms. Artman: Jim, I just want to let you know that Ken is continuing on with that. Vermont is going to be doing it. He's on the board of several organizations. I know in Florida they're doing nursing scholarships. The patient community is trying to broaden out paying for this.

Dr. Oleske: I can tell you at our school, I never thought it was going to work as quickly. But we have a Humanism Center and the CFS scholarship fit into that nicely. I would certainly recommend that as a way of going.

Ms. Artman: Kudos to Ken.

Dr. Cavaille-Coll: I don't want to appear as old fossil, but I think a part of the coordinating committee report before it became an advisory committee—and Nancy Klimas knows about that—included a session about CFS and children. I think we should try to dig up the minutes of those meetings. They are no longer on the Internet, but there was a substantial discussion at the time. The one lesson that I learned is that the big difference between children and adults is that children must go to school. The challenge of having CFS in a child is very different than the CFS in an adult, who can probably stay home and have spouse and family take care of them. There were some very important comments that were made at the time. I don't know how things have evolved as a result of that meeting, but if we do have a discussion about CFS and children, I think we do need to go back and see what we discussed.

Dr. Oleske: I appreciate that. In response, one of the reasons I joined this committee was my interest in children. I'm a pediatrician. We worked very hard in New Jersey to convince our educational department on a state level to recognize its obligations to make accommodations for children in school. Ken was also involved in that. Jon Sterling and I and one of my adolescent patients with CFS who is now going to medical school developed a lecture series that we presented on education programs and adaptation of school issues for children with CFS. We have a chapter in the monograph from New Jersey. That was the reason I originally got on this committee, to push the pediatric part of CFS.

You're absolutely right. Children are mandated to go to school and the school systems just don't understand and are very quick to blame it on early adolescence or any one of a number of things. I've already seen families investigated for child neglect and it was based on a child having CFS. It is very important to get schools to make accommodations to CFS patients. Children are mandated to go to school and the systems just don't understand.

Dr. Hartz: I have no doubt that CFS is very important for children. Adults have issues too. I've heard of some family members that don't understand. I've heard of employers that don't understand. Those are major issues and I don't think it's accurate to say that it's a greater burden for children. You didn't quite say that, but you did.

Dr. Oleske: I'm sorry. Obviously, you do what you do, and I advocate for children. I will say this: It's been a fascinating process to see an adolescent with CFS and the family dynamics. You're absolutely right, there's a lot of help and support that families need. Sometimes it's the father, sometimes it's the mother who plays the role of the bad guy who thinks the child is nothing but a malingerer. The other parent senses that there's something deeper going on. Helping families deal with that dynamic is very, very difficult.

On top of it, they have the school system sometimes not understanding at all what's going on and no accommodations made. We've been fighting that, and there are simple accommodations that can allow a child to go back to school such as a late start and two sets of books where they keep one at home and they don't have to carry those

heavy bags. There are some accommodations that the school systems have developed and hopefully, we're going to hear some of that tomorrow.

Dr. Jones: As Nancy did describe it, though, it is a broken disease in a very, very broken system. I know there were several efforts to bring the specific issues of CFS to President Obama's efforts to solicit public input and comment for the health reform effort. We just remind you as you're thinking expansively and as you're thinking about models, that there will be opportunities—we don't know quite what those are—in health reform. It's like the clearinghouse sweepstakes—you can't win if you don't enter. Where do you want to go and try to articulate that in a doable way, seizing opportunities that are already rolling that may be primed well for a disease or condition like CFS?

My closest experience is in mental health, with the first-ever Surgeon General's report on mental health issued in 1999 by Surgeon General David Satcher. There were a couple of supplement reports in the subsequent three or four years and a lot of hand-wringing and hair-pulling and declarations about what "can't possibly" be accomplished.

Ten years later, we've just issued our report on women's mental health updating the science. There's a piece for the public that accompanies that. The issues around family and the way the family views the person with the mental illness is not that much different from many of the stories CFSAC hears such as, "You'd feel better if you just chose to." Patients reported this to us consistently as we were gathering our background information.

Even moving beyond that report, in the past few months we've seen a recommendation from the U.S. Preventive Services Task Force that adolescents be screened for depression. To move in a decade from the very first Surgeon General's mental health report to a recommendation for widespread depression screening is astonishing. It took a dream. It took breaking that blood/brain barrier. That's what everyone my age and older who spent any time in clinical medicine—any aspect of it—dealt with. The brain was a private organ, a concept created over a century ago. Now we know that the brain is the master organ of so many things that happen to our bodies and plays a significant role in any number of chronic diseases. So it's not just about mental health, mental illness, and mental wellness. The brain also has these spill-over effects, if you will, and we've come to that conclusion in a decade's time.

We've been pushing at CFS since '85 and a whole lot longer and it's been challenging, but progress is still being made. The opportunities now with a healthcare system that's in convulsions and upheaval may be the opportunity that we really need. I would encourage the committee not to limit yourselves to the old thinking. Think about what these new opportunities are. The sectors where you sit, the people whom you talk to and dialog with, and the things you see can inform your decisions and deliberations. I think that's where you'll be the most helpful in your recommendations to the Secretary.

Dr. Jason: I'm really encouraged by those comments. In past we had actually talked about doing an SG report in this area. That was one of the recommendations over the

last year and a half. You suggested that we be strategic and get focused. Do you think that with the change in administration and with the new Secretary that this might be a time for us to go back and try to get an SG report on this area?

Dr. Jones: We don't have an SG nominee at this time, but the SG's office is constantly reviewing requests. There are three levels of report that the SG's office will entertain:

- The one that we know best is the Surgeon General's Report, a full scientific review; a very rigorous peer review. The average time taken to do that is about three years and the average cost is about a million dollars. It sounds outrageous, but there's a lot of public dialog and a lot of other things that go into an SG report.
- There is an SG's Call to Action, which requires a little lower level public dialog and interaction. It does not pursue the full scientific rigor that an SG's report does. It still does a science lit review, but it doesn't attempt to weigh the evidence and to try to get to what are the critical action steps.
- The third level is a Surgeon General's alert or advisory.

Dr. Oleske: We did that, just to let you know. Anand and myself and Papernik and a couple of us came down and actually met with the then-SG to advocate for the third one, which was a letter that we helped him construct that addressed a Call to Action for CFS. It was really a very positive series of meetings. Dr. Papernik was the prime mover on it. We were well-received and it looked like the SG was going to do it, but then it was decided that it was not best time for them to issue a call to arms letter. I participated in the development of the first action guidelines for HIV. That is a rigorous process and tremendous literature review, which I don't think we should contemplate. But when we do have a new SG, I would recommend that we resurrect that letter because it was pretty recent. It was only last year that we did this.

Dr. Jones: It's a process non unlike peer review because believe me, on the mental health project, we had to go back about six times because we originally did it in cooperation with the Office of the Surgeon General. We decided to part ways at one point and then just released it on our own. It's an alert or an advisory, which was this letter that the committee had approached. I think it would be perfectly reasonable to take a look at bringing the CFSAC letter back to the fore if that's the committee's desire. We may have a clearer sense of who the SG will be by the fall. That may not be an issue that you decide to prioritize, but at least list it among things that you don't want to lose sight of.

Dr. Oleske: I will send that letter around.

Mr. Newfield: In the meeting from May 2008, our first recommendation discussed the concept paper on CFS to be considered by the SG for the development of a future workshop. I don't know whether that's that third level that you were just talking about...

Dr. Oleske: That is.

Mr. Newfield: We had recommended that as our number one recommendation a year ago. We might want to consider bringing that back in terms of our concepts.

Dr. Jason: This is another example of us having rich recommendations that we probably don't need to even vote on again. We can just bring it up and take the next steps with it, because that was a fantastic recommendation.

Mr. Newfield: I agree with you, but the only issue is, in light of some of the things that have been discussed today and presumably tomorrow, we might want to incorporate those as well and make the letter more robust. Certainly we have the concept there and we probably don't need to diddle around too much with the language.

Dr. Oleske: You all should have the letter, but I'll try to pull it up so we can all look at it. It was a three-page letter from the SG alerting the American public about CFS. We were hoping to have it sent out to all doctors in the United States. I think you're right, Jason, we can probably resurrect it in the politics of the new people coming. I think it's worthwhile looking back at. We put a lot of work into that.

Dr. Klimas: It's likely to be at least one meeting away before we would go forward with the letter. That gives us the same amount of time to strengthen and bolster the provider education modules, which would have to be available to the physicians of the planet. Should we make an attempt at another national alert, it has to be linked to some sort of educational process. That CDC module that is up is lovely, but it's more of a diagnostic and less of a treatment module.

We could help work on those modules. I would be happy to work with the CDC and I'm sure I can pull other experts together from the IACFS. We'd like to see a module on autonomic, on sleep, on pain, and on other issues so that when the patients come forward, providers can get to the next level and do the appropriate treatment. If we could work together with the CAA, the CDC, and IACFS to pull together these educational modules and have them available at about the same time that the letter would be released, —it would go a long, long way to help patients access knowledgeable providers.

Dr. Oleske: That's exactly what our plan was; to have it linked to just-released CDC guidelines. You're right, that letter was going to hopefully be linked to some of the educational materials available through both CDC and the CFS Association.

Dr. Snell: A potentially productive area might relate to the economic crisis. I suspect that there will be a lot of people visiting physicians with chronic fatigue-like symptoms as a result of what's happening to them within the economic crisis.

Dr. Jones: Although last data I saw, fewer people are going to physicians unless it's really, really serious because they don't have the money for the day-to-day. So it would be interesting to see...

Dr. Snell: ...if they're turning up in emergency rooms.

Dr. Oleske: The worst place for a person with CFS is in Newark, NJ's City Hospital emergency rooms. When you go in there with the gun shot wounds and all sorts of crazy things and say, "Doctor, I'm tired and I haven't been able to work for three years," you get no service.

Dr. Jason: We should keep ourselves, as Wanda has said, to two or three targeted areas where we can really monitor them. I think that we would be missing some of our responsibility if we didn't think about what's happening with the CDC's five-year plan. We had a tremendous discussion about some of these issues at our last meeting and we've had a whole morning of talking to some of the key CDC officials. There are lots of ideas that we have generated and we need to focus on that. I think we need to respond to that in some way.

Dr. Oleske: I would agree. In fact, before coming down here I read all of the recommendations from '04 to the current time. There are a lot of good ones, and they're repeated constantly. I think we do try to do that. It's hard in a sense because we all go home and have our other busy lives that take up a lot of time.

Dr. Jones: A point of clarity: tomorrow we will have presentations in the morning on Experiences of Families, Children, and Youth with CFS, and then we'll have a roundtable presentation and discussion. We were going to have Dr. David Bell with us to discuss differentiation of CF from fictitious, invented illness or Munchausen by proxy, but he has had a family health emergency as has had to stay home. Len, he assured me that you could address the charts and slides he sent along. If I can bring those to your attention at the end of the day, I'd be happy to do that. So you would be opening with your pediatric case definition discussion and then perhaps could naturally segue into the about eight or ten slides that Dr. Bell sent along. That had been an emergent issue in both the Education and the Quality of Life Subcommittees. We are really pleased to be able to have an HHS representative from the Office of Child Abuse and Neglect in the Administration on Children and Families as well as someone from the Department of Education's Office of Civil Rights.

Public Comments

Dr. Chaunce Bogard, *Hemispherx*

I have been engaged by Hemispherx Biopharma to give them some strategic guidance on the development of Ampligen both for CFS, which I believe most of the people in this

room are award of, and—based on some new mechanistic considerations—as a vaccine adjuvant.

What I wanted to do today is give you a little bit about my background. I've been in the industry for almost 30 years. I had dozens of INDs (investigational new drugs), I've been involved with six NDAs (new drug applications)—one glorious failure and five successes launching products into the U.S. market. These have all been what I call first in class high-science sales. This is about blocking and tackling with science and clinical studies.

About ten years ago, Hemispherx approached me about coming in and helping with Ampligen. I took a hard look at it because I also had a commitment from a very large pharma company to come work. I had two kids about to go to college, so I decided that it might be more prudent to go to a place where I thought my paycheck would stay safe rather than go the other way. For about ten years, I hadn't paid any attention at all to Ampligen. Then, starting about the middle of last year, I got reengaged. I thought it might be useful to give you a little perspective from a person who's relatively experienced in drug development about what the world looked like then and now and some initial thoughts that I have.

Before I get to that, I'd like to say that in addition to what the FDA representative mentioned this morning, the FDA did notify Hemispherx late last week that we should expect our actionable correspondence sometime in the next couple of weeks. I can't comment any more than the representative can at this point.

As a result of the many programs that I've been involved with, I have developed my own ideal set of parameters and methods for a successful development. No drug or program fits them all, but the more in which you have a favorable pedigree, the better your chances of success:

1. First and most important, what is the disease awareness and the articulation of the unmet disease for the patient?
2. Is there a well-understood mechanism for the disease?
3. What's your drug mechanism; what's the target?
4. Does your data:
 - convince the FDA that the drug is safe and efficacious?
 - allow within the FDA labeling any information that allows the physicians to integrate that drug into their current standard of practice?
 - allow the payors the latitude that they need to justify the payments that they have to make?

Ten years ago when I was first looking at Hemispherx, we were dealing with a disease that there was not only little awareness of, but there wasn't even recognition that the

disease was real. There certainly was no understanding of the disease mechanism. Ampligen was a drug that had been studied in the labs of Maurice Hilleman at Merck and it was understood to be an endogenous interferon producer, but it wasn't clear how the drug was doing it or what the mechanism was.

When you have an unknown disease, an unknown disease mechanism, and an unknown drug mechanism of action, that doesn't mean you won't be successful in developing a drug, but it does mean your development cycle time will be long because you can't process a lot of information base; you're down to clinical end points.

What I see happening is the coalescence of a better understanding of the disease. There's a long way to go, but we're starting to see things that we can point to and we have a better understanding of the mechanism of the drug. I would like to bring a spirit of hope that regardless of what the short-term ruling is with the FDA, we'll see a much better breakout in trying to modulate this disease. I just wanted to give the perspective of a person who thinks that there will be hope on the way in understanding the disease.

When I think of what's the most important thought I could give back to the committee, it really all starts with disease awareness and the articulation of the disease. Everything I heard today was about funding. When there's a greater awareness that this is unmet disease, the funding will come and with funding, all the other things can be dealt with.

I would like to commend the CDC on its "Missing My Life" ad. I've been in this industry a long time and that's really a very good ad. Do you have any ways of tracking? Do you really see how effective that is? It's one thing to count how many times you see the hit, but can you use those surveys to see if it did impact people's beliefs and perspectives on the disease? With this information, I can tell you what you might have to do with it.

Marly Silverman, Founder and Public Policy & Community Advisor, Patient Alliance for Neuroendocrine-immune Disorders Organization for Research and Advocacy Inc. (P.A.N.D.O.R.A.)

Accompanying Document: *Response to Request for Input – April 27, 2009: CDC Five-Year Strategic Plan*

Thank you so much for this opportunity. This has been a most amazing meeting. I am so pleased to see behind me tables full of testimony from individuals, patients, stakeholders, care givers and interested parties coming through for us. We have come a long way. I have been attending these meetings for the last six and a half or seven years and every time I come here I am overwhelmed with emotion and deep gratitude.

First of all, I would like to dedicate this testimony to some of the folks who are no longer here with us:

Jerry Crum
Steven Croft, a family physician and rheumatologist

June 8, 2008

who took care of me and some other patients in Florida	February 16, 2009
<u>Taffy Todd</u>	April 28, 2009
<u>Sophia Mira</u> , a young woman who was actually sanctioned by the medical profession in England, died at age 32.	November 25, 2005
<u>Lynn Gilderdale</u> , died at age 31 in England	December 4, 2009
<u>Sharon Kirk</u> author of <i>When I Cry Wolf: A Society Lost to Chronic Fatigue Syndrome and Mold</i> , former professor, La Salle University	March 3, 2009

- Please help us to reunite Brian Baldwin with his family. I believe tomorrow the topic will be the issue of CFS pediatrics and the issue of Munchausen by proxy that has plagued the CFS parent community. This is a serious case. We can no longer just be blind to what's happening out there.
- I would like to thank the Patient Care/Quality of Life Subcommittee chaired by Rebecca Artman, the NIH, Dr. Wanda Jones, and the Department of Health and Human Services representatives here for their generous grant of this one-time broadcast that I hope will be repeated. This has been a dream come true for P.A.N.D.O.R.A. As you are aware, every time that we have come here, we took part in the Empty Chair Project by putting pictures of CFS patients on the empty chairs behind me. Today I am pleased to say that I do not have to do this. It is such a wonderful thing to feel and experience.
- I would like to make a comment about Dr. Kenneth Friedman. Unfortunately he was not able to be here. As you are aware, Ken is the Director of Public Policy for P.A.N.D.O.R.A. and I am so pleased to have Ken on our team. We have done some great things recently. In addition to the New Jersey CFS medical student scholarships, we have also now provided scholarships to Vermont. On May 12, the University of Vermont received a grant that P.A.N.D.O.R.A. provided through the Vermont CFIDS Association. I'm very proud of that.
- We also provided a grant for the translation of the Physicians' Manual into Spanish. That same manual has also been translated into Japanese. The manual was developed by Ken Friedman and other doctors, including Dr. Oleske in New Jersey.
- I need to ask you all, including the IACFS, for assistance in updating the manual with more information, including in the area of pediatrics. Right now I have the Spanish organization that I gave the grant to on hold waiting for these updates. We need to get that going; otherwise my money is going to go away.
- Pandora has been actively pursuing in the state legislative area a neuroendocrine-immune research center or institute. I have discussed this with other stakeholders in the community, including those in Reno, NV, in order to form a national alliance to advocate for a center. The CFS research centers are

important for our community, for CFS patients, and for physicians. The input that we provided to the CDC, which was written by Dr. Friedman, Rebecca Artman, and myself, included everything that you have discussed plus more. I was disappointed because I did not hear Dr. Bill Reeves discuss our input. He only talked about what the CDC is doing. I would like to get some feedback on our ideas.

Thank you and keep up the good work.

Jennifer Spotila

Accompanying Document: *Comments by Jennifer Spotila, delivered via telephone to the CFSAC on May 28, 2009*

Thank you Dr. Jones and Dr. Oleske for the opportunity to speak to you by phone today. That's the only way it would be possible, so I do appreciate that very much.

Every six months or so, the Advisory Committee hears reports from Federal representatives, along with testimony from patients and advocates. Every six months, you make recommendations and then you return to your offices to deal with all the other issues that demand your attention.

For the Federal *ex officio* members of the committee, that means work on a wide variety of health priorities including pandemic flu, HIV/AIDS, heart disease, food safety, and bioterrorism. Let's face it: your work requires you to put out fires across the public health landscape.

But let's face something else: CFS is not one of those fires. Not to your agencies or to HHS. I doubt very much that any Federal employee in that room has a boss who regularly asks you, "What do I need to know or do about CFS today?" This lack of urgency is pervasive throughout the department, and it hampers the work of the CDC, NIH, and the work of the advisory committee itself.

I call your attention to one example, which others have noted today. There are 215 illnesses and conditions listed on NIH's Estimates of Funding. Out of those 215, only one line item is projected to have less funding in 2010 than in 2009: CFS. One out of 215. CFS funding is projected to drop from \$4 million in '09 to \$3 million in 2010. This 25 percent cut in funding—especially when no other category is being cut—is emblematic of this entire department's lackadaisical approach to CFS.

We frequently hear from NIH, as Dr. Hanna said today, that the funding level is dependent on quality grant applications coming in first. I suppose we should conclude that the NIH is overwhelmed with quality applications for research on Pick's Disease, which affects fewer than 200,000 people in the United States, because that category is projected to receive a 30 percent increase over its funding in 2008. I don't believe that the members of this committee should be satisfied with that explanation. Even if the

CFS funding level stayed the same—even if it was increased by 25 percent, you know that this is in no way proportional to the burden of CFS on our economy and our people.

This paltry response is possible because CFS is not seen as a real public health crisis. Patients and advocates make many requests for action at these advisory committee meetings. We ask for big solutions on a short timeline. There are many barriers to solving CFS, and we want you to help remove them. But we feel like our public health agencies are fiddling while our own Rome burns down.

I make one request of this committee today. I ask that in cooperation with Dr. Jones and her staff, you brief Secretary Sibelius on CFS to inform her that it is a public health crisis requiring her personal attention and the attention of the department.

You have the collective knowledge that CFS is a devastating illness. And you also have knowledge that CDC and NIH are not investing research dollars in proportion to the burden of CFS. This knowledge creates obligation. It is your obligation, as a committee, to ensure that the Secretary is fully briefed with this same information about CFS.

You must push for awareness and action within HHS because no one else can. The basic premise of this advisory committee is to ensure the department is doing what is necessary and what is right to solve CFS. In order to do that you must first gain Secretary Sibelius's attention. My single, simple request of you today is that this committee put CFS on the Secretary's radar. Until Secretary Sibelius recognizes CFS as the crisis that you already know that it is—until word comes from the top down that CFS is a fire—I fear nothing else will change.

Thank you for this time.

Alyson Butcher

Hi, thank you for having me. My name is Alyson Butcher and I flew in from Houston, TX, to be here. I am also happy to have my parents from Washington, DC, and my cousin from Modesto, CA, here to support me. I'm a CFS advocate and patient and I do what I can to give a face and voice to the many CFS patients who are too ill to leave their homes.

I'm 30 years old and I've had CFS for my entire adult life, but I've only been officially diagnosed since 2005. It took four years and four doctors to get finally get diagnosed. My original plan today was to come and sit in on the entire advisory committee meeting but my plans were foiled by my disease. This morning I woke up, ate breakfast, then took a five-hour nap. I'm just happy to be here.

My disease is a great frustration. This weekend my husband and I celebrated our fourth wedding anniversary at Disneyland. The only reason I survived the weekend is because my husband pushed me around in a wheelchair for both days. I could go into

how this disease has affected my quality of life and my marriage, but that would take more than five minutes.

I'm here today to give you a sense of urgency. Not enough progress has been made in the education of physicians and other healthcare professionals or the public. My own mother-in-law, who is a registered nurse, does not understand CFS even with me talking to her about it. The doctors I went to before finding my current one were skeptical at best and completely dismissive at worst when I proposed the possibility of my having CFS. More needs to be done more quickly on all fronts: education for healthcare professionals and the public, research, diagnosis, treatment. I am a willing guinea pig. I would gladly give samples of my blood and go through as many tests as you want to help get to the root of what causes this disease and how we can treat it and deal with it. But I've never had that opportunity. I've already lost my 20s. I don't want to lose my 30s. Again, I want to give you a sense of urgency. We need to move forward more quickly.

Thank you very much.

Barbara Bell

Accompanying Document: *written testimony*

Hello. I'm Barbara Bell. I'm from Manassas, VA. Thank you for this opportunity to speak. I hope you can forgive me for reading right off the page. My master organ, as you called it, is very foggy right now.

I'd like to talk about the emotional and sociological effects of CFS. Healthcare practitioners, particularly those in mental health, need more education in this area.

CFS leads to profound loss. It can make or break a marriage. Sick parents may lose custody of their children. It often leads to career death, financial insecurity, and an uncertain, scary future. Friendships lapse because we can't keep up with them or illness makes them uncomfortable. We may have to give up pets. We may lose our independence. Self esteem, self worth, and self respect are shaken. Our self identity is challenged. Depression often follows. People with CFS almost always suffer protracted grieving that may last for years because all of the losses we experience are compounded by physical misery. We may not all experience the exact same losses, but we all grieve our former lives. We grieve being able to take energy and health for granted. We grieve being able to go out with friends or do anything extracurricular. Sometimes even talking to a friend on the phone takes more energy than we have.

We become frustrated and angry with our limitations. We push beyond our limits because we don't want to accept our losses. We blame ourselves for not trying hard enough or in the right way. Many of us feel despair and even suicidal feelings at some point. Finances are a dark cloud hanging over most of our heads, especially those of us who are single, jobless, and praying that Social Security will move quickly and in our favor. We often have to forego treatment because we can't afford it. And to add insult

to injury, stress makes CFS symptoms worse. And everything that I'm describing is extremely stressful. So we're chronically stressed.

This illness is very isolating. Most people, including doctors and mental health professionals, have no idea how profound the effects of CFS are on our lives. Many don't believe it's a real illness. Certainly not a serious one. We're often told that we look fine or good or healthy. Some say we're hypochondriacs or faking it. Lack of understanding leads to conflict with friends, family, bosses, coworkers, doctors—pretty much anyone we have to interact with. Loved ones feel slighted because we don't spend enough time with them. They become resentful when they have more chores to do than before. They feel helpless and guilty. We feel helpless and guilty. And these negative emotions often come out as aggression or passive aggression and the cycle of social stress continues.

Current education efforts focus primarily on physical symptoms and diagnosis, which is very important. But it's crucial that healthcare providers of all kinds understand these far-reaching effects of CFS on a patient's emotional well being. That's especially true for mental health providers, who are trained to help patients with coping and self esteem. But they can only do so when they're aware of the physical and psychological issues at hand. Physical and emotional well being are linked. Treating both will have a greater effect than just treating one. It's vital for patients to hear that they are believed, that it's okay to grieve, that what they feel is normal and expected, and that there's no shame in asking for help. We encounter so much invalidation that a little bit of validation can go a long way.

Thank you for listening.

Craig Maupin (via telephone)

Accompanying Document: *written testimony*

My name is Craig Maupin and I've had CFS for 20 years. I have several points and my points are pertaining to the strategic plan that was laid out by Dr. Reeves:

1. My first point is that I couldn't help but notice Dr. Reeves' summary of the Atlanta stakeholders meeting. Having listened to that meeting, I felt Dr. Reeves misrepresented the input. The input I heard at the meeting really challenged the objectivity of the CFS program and it challenged whether the clinical picture of CFS at the CDC is accurate.
2. My second point is that the 2008 review panel does not reflect a diversified group of theories about CFS. Dr. Reeves described Dr. White as an expert on autonomic dysfunction. In Atlanta, he described Dr. Lange as a "neurologist." These researchers are classified as a psychiatrist and psychologist, respectively.
3. My third point is in regard to Rebecca Artman's question that we heard earlier. I can't imagine why Dr. Reeves would choose to collaborate predominately with psychiatrists for what he refers to as a non-psychiatric illness. In Atlanta Dr.

Reeves mentioned the phrase that the CDC needs to “walk the walk.” I felt that his answer to Ms. Artman did not correlate with his walk.

4. My next comment relates to the objectivity of the CFS program, and we certainly heard a lot about that in Atlanta. In 2006, the CDC held a press conference on CFS. At that press conference we heard different interpretations from the CDC/CFS research team. One perception from a female researcher who is no longer with the CDC was as follows:

She said: “We’ve been able to show that CFS is very heterogeneous, it’s not just one thing...We’ve actually demonstrated that there are probably four or five molecular profiles or groups of people that make up this complex...”

At that same press conference, Dr. Reeves portrayed the study conclusions very differently. He said: “This study demonstrates that the physiology of people with CFS is not able to adapt to the many challenges and stresses encountered throughout life.”

Those are two very different pictures of the interpretations of the research. I think it goes to the heart of responsible stewardship of the CDC to make an announcement that’s based on a full study. They made that announcement based on a pathology-specific design. My question is why wouldn’t it be better to wait for a study that allowed for the entire genome before making such an announcement? Or at least proceed when journalists had access to the other findings of the study?

In that same vein—and this pertains to the five-year plan—Dr. Reeves earlier talked about educating physicians and the public about prevention and control. Why not wait until studies have been published by the CDC on prevention and control? It seems to me unusual that we’re going to begin educating clinicians before we have investigated the material. It’s putting the cart before the horse. Nobody made that point. I think it’s an important point.

Dr. Jones, you earlier made the comment that this committee sees CFS through a gendered lens. I can’t imagine how this committee can’t be concerned about some of the papers we’re seeing come out of Emory University if it sees CFS through a gendered lens. We’ve seen papers attributing CFS to a response to child abuse. We have seen papers attributing CFS to a response to disasters. These are not the kind of papers that you see from a program that would be immune to bias towards women’s illnesses. These are exactly the kind of papers you would see from a program that would be affected by biases towards women’s illnesses.

I do have several recommendations and I think some of you touched on these earlier. I think the CFS program needs to foster inclusion of researchers who espouse other theories. I think Dr. Glaser touched on that. Dr. Klimas touched on that—the need to include researchers who have theories beyond stress response.

Dr. Jones: One minute.

Mr. Maupin: Ok. To wrap up I would like to say that CFS patients are not concerned about overall amounts of output and they're not concerned about overall spending levels. They are very concerned about the objectiveness of CFS research and they're concerned about openness to all theories and about an accurate picture of the illness being portrayed. And so my hope is that the committee will focus on those issues.

And I'd like to thank the committee for the time that they've given us. I notice that each of you missed lunch and I know you love lunch as much as I do. That's quite a sacrifice. I'd like to say thank you for the work you're doing. Thank you.

Kathryn Stephens

Good afternoon committee members, Secretary Sibelius, and Mr. President. My name is Kathryn Stephens, a patient of 21 years and a previous support group leader. I come here today with hope, but also with trepidation because this committee has been worthless since its inception. I have a list of whys today:

- Why has no one questioned the CDC's erroneous demographics, which are based on their equally wrong research criteria?
- Why do you and the CDC ignore the Canadian criteria or the WHO's (World Health Organization) diagnostic code of 93.3? We have CFS according to the '94 criteria in the U.S. It's ME, a neurological condition.
- Why have so many committee members since the panel's inception been so uninformed, so ignorant of the more than 3,500 studies that have found serious abnormalities in so many people you see?
- Why do you exist?
- Why have the international associations for CFS/ME correctly changed their focus to ME while you have not? Are you part of the CDC's denying and obscuring of the reality of CFS? Do you support their international focus, meaning the UK's NICE guidelines? Are you even aware of those?
- Why has the CDC tried to copy the UK's guidelines, which make this a psychosocial illness and which prescribe CBT and GET? William Reeves must go and now, before more irreparable possible malpractice harm has been done.
- Why is a perfect example of how behind the research and understanding you and the related Federal sites are allowed? The AHRQ website is indicative of the problems inherent in the CDC's hiding the true facts of this terrible disease. Their website is dated September 2001 and it makes this statement: "This evidence report has not been updated within the past five years. It is maintained for archival purposes only." Can you believe it? Why?

It goes on to say that, "the validity of one case definition over the other is not well established" and "there are no clear biologic markers" and "no effective treatment specific to CFS has been identified." These nine year-old statements are still true today at the CDC. How can that possibly help? What does the CDC ever

investigate that is replicable and valid? What has this committee accomplished for the sick and dying? The site then has the audacity to conclude, “Although several therapies have been studied, potential benefits as well as harm are not well established and behavioral therapies that emphasize increasing activity levels may improve quality of life and function.”

Most dedicated researchers know that these are damaging statements. The **nine** studies that the website reviewed did not have any patients who were too sick to be included. It’s not fatigue that is the problem. It’s neurological damage and recovery from activity. If CFS has no scientific basis as the CDC claims, why should there even be a CFS department of the CDC, which now includes traumatized children, depression, fatigue from dozens of causes, and God knows how many other inclusions? This current program must go and Mr. Reeves should be allowed to move on to a new, competing interest at Emory.

- Why do I think this comment may be in vain? That you will allow this horrible disease to be a psychosocial illness? Maybe a class action lawsuit or a Congressional inquiry will help you understand how serious we are about action now. I will thank you when and if informed and constructive action takes place for the concerns that we collectively will have expressed here today and tomorrow. We’ll all be thankful then.

[During a dialog about the availability of written testimony, Ms. Stephens thanked Dr. Jones for all of her hard work.]

Denise Swanteck

Accompanying Documents: *Memo on CFSAC testimony; CFS Research email*

I am a CFS patient. I wasn’t diagnosed until 2004, but I have had it 14 years. There are probably a good many people not getting diagnosed, and then there are problems with people getting treated, for many reasons.

I’m concerned about funding. CFS patients average four dollars per patient compared to other disorders and diseases, and that’s basically just enough to buy somebody a get well card. My concern, as with many other patients, is increased funding for research, but also for public advocacy. The public doesn’t really understand CFS. There is some dispute about the definition. I know that the CDC has a definition that is supposed to be accepted by the medical community, but there’s still some dispute about that. The public certainly seems to be misinformed, if not completely in the dark, about that.

As a CFS patient, if you choose to tell somebody, it’s hard to in anyway accurately describe the disease other than to give a list of symptoms—that’s what a syndrome is—or a long technical definition. I know that internationally there’s some dispute about what it is. There’s probably more agreement about the WHO’s definition than the CDC definition in this country.

Also, there's anti-viral research. I know that Ampligen is up for approval again at the FDA, and that's been a long time coming. There are several other drugs that aren't getting any insurance coverage because the FDA hasn't approved them for CFS.

CFS exists as far as Social Security and the government go, but the medical community at large and the research community still have a long way to go. And research funding and advocacy funding for public education would go a long way in correcting that. The funding should be spent on clinical research into the causes—although the causes can be many or multiple—instead of psychological research. Only a small percentage of the papers get approved because of the money. There was talk of centers of excellence in a multi-disciplinary form, but as far as I know, they started to get off the ground and then pretty much had their plug pulled. I still think that's a good approach and worthy of research funding.

Geographically, there are too few doctors who actually specialize in CFS. They are distributed throughout the United States, but really, you're talking maybe ten or less. The centers of excellence, if they're located in the right place, would really help people. Based on clinical research, if you have to travel more than an hour and a half each way to get Ampligen, it probably negates the positive effect of the drug. Geographical distribution, I think, is important.

I know that there's a genome study that's been done. A lot of the work is being done in England. The genome research is important because CFS has multiple triggers. It should have the same respect as multiple sclerosis and other diseases that don't have a known cause.

There's a huge economic cost. To each family with a CFS sufferer, the cost to the public in disability and the economy is much greater than people realize. The numbers of sufferers are probably underestimated because so few people get diagnosed and when they are diagnosed, many of them can't afford to be treated.

Dr. Oleske: I think we've had a good day. We've heard some tragic stories and I wish that we could be quicker in our response and give more time to those individuals, but I appreciate everyone carefully listening. Everyone should have gotten a copy of the written testimony. I would suggest before retiring, you make sure you read them. I think hearing them is one way, but I think we need to give them the courtesy of reading something that they probably put a lot of time and effort into when they could ill afford that effort. We convene tomorrow at 9 a.m.

Dr. Jones: We will have some minor subcommittee logistical items related to your travel and other support that we would like to take care of at breakfast so that we don't waste public time. If you could be there at least by 8:30 a.m. so that we can make sure that we've got what we need and everything is in order for you. Members and the public, check in at the desk and you'll be escorted upstairs. Thank you all very much for attending.

Dr. Oleske: I want to thank representatives of the various agencies. It takes a tremendous amount of time and effort.

Adjournment

Thursday, May 28, 2009

Call to Order/Opening Remarks

Dr. James Oleske

Dr. Oleske called the meeting to order. Noting the day's full agenda, he remarked that perhaps CFSAC members can "take some of the honest introspection from yesterday and turn that into prospective plans for how we can help move the treatment, care, diagnosis, and maybe someday prevention of CFS." He said that the morning's agenda in pediatric CFS "is very close to my heart," because he began his involvement with chronic fatigue by treating young adolescents.

Dr. David Bell's cancellation allowed some flexibility in the day's agenda, said Dr. Oleske, suggesting that any extra time be spent on public testimony.

Roll Call, Housekeeping

Dr. Wanda Jones

Dr. Jones reminded Dr. Oleske that the CFSAC subcommittees gave up their lunch meeting the previous day. Subcommittee members were anxious because they had not had focused time to prepare recommendations and sound each other out on the day's presentations and discussions. Dr. Jones added that CFSAC had already expanded the public comment period and that any extra time in the agenda would be allotted to the subcommittees.

Dr. Jones noted another change in the day's agenda—the addition of an open session between 1 p.m. and 2 p.m. with Dr. Cheryl Kitt, Deputy Director of the Center for Scientific Review. Dr. Jones suggested that the committee take an early lunch, use the extra time for subcommittee business, then reconvene for the open session with Dr. Kitt.

Dr. Jones then conducted the roll call. All voting and *ex officio* CFSAC members were present.

On a final housekeeping note, Dr. Jones noted that in addition to the rest area at the back of the room, a table would be available for community members who might need to sit and put their head down.

Pediatric CFS Case Definition

Dr. Leonard Jason

Accompanying Documents: *Material submitted by Dr. David Bell for the 5/28/2009 U.S. Department of Health and Human Services Chronic Fatigue Syndrome Advisory Committee; DePaul Pediatric Health Questionnaire; Table 1: Preliminary Model for a Medical Case Definition of ME/CFS; A Pediatric Case Definition for Myalgic Encephalomyelitis and Chronic Fatigue Syndrome*

Dr. Jason: I'm going to start by going through the material that David Bell was going to present. He initially was going to talk about the IACFS/ME pediatric case definition. I'm going to hold off on that until I cover the second part of his presentation providing background on Munchausen syndrome. Munchausen's is a type of factitious disorder, which in turn is classified as a somatoform disorder.

Somatoform disorders are characterized by physical symptoms—pain, nausea, dizziness—that mimic disease or injury for which there is no identifiable physical cause. The physical pain symptoms that a person feels are related to psychological factors. The types of somatoform disorders are:

Somatization Disorder

- History of somatic symptoms before age 30.
- Pain occurs in at least four sites of the body. An example is gastrointestinal pain unrelated to vomiting and diarrhea.
- One sexual problem arises, such as lack of interest or erectile dysfunction.
- One pseudo-neurological symptom appears, such as fainting and blindness.

Conversion Disorder

- Presents when a patient has neurological symptoms like numbness and paralysis.
- Symptoms arise in response to difficulties in a patient's life.

Hypochondriasis

- Excessive preoccupation or worry about having a serious illness.
- If there is a medical illness, patient's concerns are far in excess of what is appropriate for the level of disease.

Malingering

- Fabricating or exaggerating symptoms of a mental or physical disorder for a variety of motives, such as to avoid work or to get out of going to school.

Dissociative Disorders

- The failure to integrate information about one's personal identity, memory, states of consciousness.
- Examples are:
 - depersonalization disorder—feeling detached from the body.
 - dissociative identity disorder—the presence of two or more distinct identities.

Factitious Disorders

Munchausen's Syndrome is the most extreme variation of factitious disorders. It presents as the intentional fabrication of a physical or psychological symptom in order to assume a sick role. This differs from malingering, where a person fabricates the symptoms of an illness to reach an external goal, such as avoiding jury duty. In Munchausen's, the person deceives the healthcare professionals into believing he or she is ill. The person migrates from hospital to hospital attempting to get admitted by continually faking or producing symptoms of illness.

DSM (Diagnostic and Statistical Manual of Mental Disorders) IV abandoned the term "Munchausen's" in favor of "factitious." The American Professional Society on the Abuse of Children uses the term pediatric condition falsification (PCF) for the diagnosis of the child. The most common symptoms include bleeding, vomiting, seizures, fever, and rash.

Factitious disorder by proxy (FDP) is used for the adult (perpetrator) and is considered a form of child abuse. Usually it involves the mother. An example is putting blood in the child's urine. One theory is that the parent who engages in this activity is looking for attention, specifically the attention that the parent of a chronically sick child can garner.

This is a very difficult disease to diagnose. You certainly have to interact with the child and the parent to make a diagnosis. Two examples are:

- You actually observe or you videotape the caregiver harming the child.
- The child improves when the parent is not around.

Children with ME/CFS often do have impaired school performance. One study suggested that ME/CFS might be responsible for as much as 50% of long-term absences from school.

There needs to be a lot more data about PCF as well as ME/CFS. There's a lot of skepticism in the medical community towards ME/CFS. That increases the skepticism that sometimes gets translated to educators. That's what sometimes provokes the problem.

- ME/CFS needs to be a diagnosis that specifically excludes PCF (FDP).

- This information needs to be distributed to pediatricians, child abuse agencies, and educators.

Pediatric CFS Case Definition

We have a sense of what PCF is. Now we want to differentiate it clearly from what is ME/CFS. As we know, the Fukuda case definition was developed for adults. We believe that it might not be appropriate for children and adolescents. The IACFS developed a pediatric ME/CFS case definition in 2006 and released it in 2007.

- We basically incorporate the structure of the clinical case definition developed by Caruthers. It requires certain symptoms to provide more specification of clinical symptoms. So, the Fukuda definition is more polythetic, where you pick four out of eight symptoms. The Canadian criteria say you have to have specific symptoms.
- In addition to developing the construct—what symptoms you want to look at—it's critical to develop an instrument to actually go along with that construct. We developed what's called the DePaul Pediatric Health Questionnaire. Copies are included in your handouts.
- We also have a one-page flyer of next directions that tries to make a biological parallel to each of these self-report symptoms. This is one of the things that Nicole Porter and our group at DePaul are trying to do—explore how to look for biological confirmation of all the self-report information that we'll be talking about today.
- Children 12 or older generally fill out the questionnaire themselves. Those 11 or younger fill it out with the parent. Medical examination needs to occur to rule out any other cause of the illness.
- It's not enough to define a construct with very specific exemplars of what it means, which we tried to do, and develop an instrument that has some reliability. The important third step is to collect data on the instrument. We had several physicians who are extremely knowledgeable about this illness refer patients—both healthy controls and individuals they thought had ME/CFS.
- We had 54 people who came into our sample. They had a medical examination and filled out the self-report questionnaire.

Diagnostic Criteria

We tried to diagnose the people two ways—using the adult Fukuda criteria and the new pediatric criteria. These have some implications for the adult classification as well:

1. Unexplained persistent or relapsing chronic fatigue over the past three months (as opposed to six months for adults) that:
 - Is not the result of ongoing exertion.
 - Is not substantially alleviated by rest as defined by the 2003 revisions that we've talked about in past sessions here.
 - Results in substantial reduction in previous levels of educational, social, and personal activities.

2. Specific symptoms in five classic areas that have persisted or recurred during the past three months but may predate the reported onset of fatigue (symptoms are not counted in the adult definition if they predate the fatigue):
 - Post-exertional malaise must occur with the loss of physical or mental stamina and rapid muscle or cognitive fatigability.
 - Unrefreshing sleep or disturbance of sleep quantity or rhythm.
 - Pain.
 - Two or more neurocognitive manifestations.
 - At least one symptom from two of the three subcategories: autonomic, neuroendocrine, immune.

An individual could lack the three classic CFS symptoms of post-exertional malaise, cognitive problems, and sleep disorders and still have four of the other eight Fukuda criteria. That's a potential problem. With the pediatric criteria, you have to have all of them. This produces a very homogeneous group that meets all these symptom criteria. It's a very sick group of kids.

We rated the symptoms in terms of moderate or severe and their frequency in terms of at least half the time or more. Patients had to meet criteria in terms of frequency, severity, and duration for it to count.

- Sixteen of the 35 kids met full criteria for the severe ME/CFS group. This group is extremely disabled. It's a very homogenous group. I would consider this the group you really want to use for research purposes.
- Fourteen kids met the criteria for what we called "moderate." In other words, they didn't meet all the criteria. You might think of this as a clinical group. They had four out of five of the classic ME/CFS symptoms and they only had one in the autonomic/neuroendocrine/immune manifestations. This group of 14 kids, if you compare them with the severe group, is significantly different on many of the symptoms. You don't want to say they can't use the CFS label. They still are very sick, but they're not as sick as the severe group.

Committee Discussion

Dr. Glaser: You are dealing with a group that has a significant age range and the immune system is maturing over time. Can you find differences if you do the analysis based on age?

Dr. Jason: That's a good question. We haven't done that yet, but it's worth doing. If you think of the prognosis in children versus adults, there really is a different prognosis.

Dr. Hartz: You mentioned that in terms of comparing the severe and moderate group that the differences were defined on the basis of autonomic, neuroendocrine and immune manifestations. In what other ways was the severe group defined as "severe"?

Dr. Jason: The severe group tends to be home more and do home schooling. The moderate group tends to be able to go to school part time. You see indices of disability. You see that one group is more impaired, the other group less impaired.

In terms of other arenas, my guess is that just about any arena you look in, you'll find differences in those two categories. If you don't meet the case definition of high CFS idiopathic chronic fatigue, we really don't know much about that group, which is a problem. That group could be extremely interesting.

Whether you meet severe or moderate—research case definition or clinical case definition—we want to understand this entire entire group, not just the group that's the homogeneous group. They're all worth us understanding, but for research purposes, let's get them as tight as possible. That's the difference with these particular strict criteria versus something that's polythetic where you get four out of eight symptoms. That's the difference.

Dr. Hartz: Did you create other moderate groups that had the autonomic symptoms but did not meet symptoms in the other categories? Were there groups like that?

Dr. Jason: There are some other groups, and I'll talk about that in a second. They do not meet the strict criteria for the research group, but diagnosis of CFS can still be made. With this system, you can meet either the clinical (less strict) or the research (strict) criteria. CFS symptoms and severity can wax and wane.

Dr. Papernik: I'm not sure I understand. In the beginning you're saying that you have strict criteria for making the diagnosis of CFS/ME in children. Then you say that maybe the definition is not so strict at all. Maybe you have people who fully meet the criteria and people who don't fully meet the criteria. Is that what you're trying to say?

Dr. Jason: Absolutely.

Dr. Papernik: But then how do you have strict criteria?

Dr. Jason: Strict criteria for the research group.

Dr. Papernik: So in clinical practice what you're saying is that people don't have to meet the full criteria for pediatric ME/CFS.

Dr. Jason: Absolutely. Think of someone coming into your office who doesn't have four symptoms for some reason. One symptom may have predated the illness. The person says, "I really want a diagnosis of ME/CFS." You say, "You don't have the four symptoms. You have three symptoms. You don't meet the criteria." We wanted a homogeneous group for research purposes, so we set strict criteria for that and variable criteria for idiopathic chronic fatigue. Under this system we say, "You meet the clinical criteria." We're trying to differentiate those two groups.

We're saying that this is an illness that remits at times and gets more severe at times. This is also true of many characteristics of MS. At the time you catch CFS, it's important to differentiate whether it's moderate or severe enough to meet the full case definition. If it's that severe, those are the ones that I say researchers should be capturing and studying. That doesn't mean that we shouldn't be studying the other ones. It means that the severe group is going to be more homogeneous.

Dr. Papernik: I guess when people say "criteria," it raises a different type of reaction in me when I'm looking at patients and trying to make a diagnosis. When I see somebody say, "These are the criteria to make the diagnosis," it means that if you don't meet these criteria, then you don't have this diagnosis. It may be semantics, but maybe when we're talking about the clinical criteria, they should be called guidelines instead of criteria, whereas for a research tool, they should be criteria.

Dr. Jason: We're suggesting a way to get a homogeneous group in order to study this illness. We think that a severe group is the group that we should be trying to identify. For clinical purposes, the moderate group probably also has the illness, but it's probably a more differentiated illness with more variation. We use the ME/CFS pediatric criteria, but the moderate patients don't meet the full criteria of the severe group.

- In addition, there's atypical ME/CFS defined as experiencing three or more months of fatigue and having two or three of the classic five ME/CFS symptoms. Two children met the criteria for atypical. We absolutely believed that they had the illness but they didn't have all the criteria and we put them into that category. Again, for research purposes, we probably wouldn't be putting them into some of our pathophysiological studies, but we certainly will allow them to have this label because we thought they had the illness.
- There's also a category of ME/CFS-like, meeting all classic ME/CFS symptom criteria except they didn't have three months duration or they lacked a medical evaluation. One participant had experienced fatigue for only two months but expressed the other major symptom criteria.
- One child was classified as ME/CFS in remission, meaning the person met full symptom criteria at one time but was not experiencing symptom etiology at the time of the study.

For these purposes, we put the individuals who had severe, moderate, and atypical into the new pediatric case definition. We said that participants classified as ME/CFS-like and in remission did not have ME/CFS.

Fukuda criteria were analyzed versus the pediatric criteria. We used what's called the receiver operating characteristic. The bottom line is that of the 33 cases referred by physicians, 25 were identified with Fukuda strict criteria, 32 with our ME/CFS pediatric criteria. **We believe that the pediatric ME/CFS criteria are more accurate in correctly distinguishing between the presence and absence of pediatric ME/CFS.**

What does this mean?

- If you have criteria (Fukuda) that evidenced 76 percent sensitivity and 100 percent specificity, you'll miss 24 percent of patients with the illness.
- The pediatric criteria have 97 percent sensitivity and 100 percent specificity, which means that you would only miss 3 percent of patients.
- In a population with a low illness prevalence, the risk of under diagnosis is a key concern. It's important for a diagnostic tool for a low prevalence illness to have high sensitivity and negative predictive value.

The Fukuda criteria as it's stated missed cases due to these reasons:

- The Fukuda criteria required a duration of six months. The pediatric criteria required a duration of three months. That was one of the critical reasons that kids did not meet the Fukuda criteria.
- The Fukuda criteria stated that the concurrent problems such as sore throat and concentration problems must not predate the fatigue. This also led to the unnecessary exclusion of children who did in fact, we thought, have the illness. The new pediatric criteria recognized that in children with insidious onset, such symptoms may predate the fatigue.

Eight participants received a physician's diagnosis of ME/CFS but did not meet the Fukuda criteria. Each of these eight children experienced symptoms from all the major categories including fatigue, post-exertional malaise, pain, neurocognitive difficulties, and autonomic/neuroendocrine/immune manifestations. We think these children had this illness, but the Fukuda criteria were not picking them up.

The Fukuda criteria are the most widely used diagnostic measure to diagnose ME/CFS in both adults and children. These criteria have a high likelihood of under diagnosing pediatric ME/CFS cases from our experience. And by the way, this is not a funded study. It isn't as large and as nice as we would like, but I think it does prove something—that this new pediatric ME/CFS case definition using both moderate and severe criteria and a reliable instrument to assess them could lead to more adequate diagnosis of youth with ME/CFS.

Committee Discussion

Dr. Papernik: What's your definition of "pediatric"?

Dr. Jason: Under five years of age, you would say that it's hard to use any of our instruments and it's hard to make assessments. Certainly there are children who are younger who have this illness, but at least in terms of the children who we've seen, we go from about 5-17.

Dr. Hartz: In order to calculate sensitivity and specificity, you need to have a gold standard. My impression is that you used the pediatric criteria as your gold standard. If you use the pediatric criteria as your gold standard, it's obviously going to look very good and anything compared to that will be less good. Did you have some other way of identifying patients with CF other than the pediatric criteria?

Dr. Jason: How you define a gold standard is a difficult issue. The way we tried to do it was to select three people we thought were some of the most knowledgeable in the world about ME/CFS, ask them to identify people in their practice whom they thought had the this illness, and request that they refer these patients to us. That's how we created that gold standard.

Dr. Glaser: As you know, in North America, we don't become EBV positive as a population until sometime in the mid-teens. In any of these pediatric groups, are you seeing that even the younger kids are EBV positive? In those instances where Cyclovir might have been used, is there any evidence within the age groups that there are different responses to taking Cyclovir?

Dr. Jason: There is a study that is just now finishing and being published in Chicago that Renee Taylor has been involved with. She got several hundred kids who had mono in childhood, then followed them for several years. She's just now beginning to publish some of the data on that. I think it's going to be a very important study looking at which kids end up developing ME/CFS. I would say probably one study has been published on that cohort. The questions you're asking involve some other studies that are going to be coming out with. The issues you're talking about are critically important. For our particular study, we're not looking at treatment issues, we're doing diagnostics.

Dr. Papernik: In Renee's study we did not use the pediatric definition, from my recollection.

Dr. Jason: It's possible that you were not using that particular case definition but the people at Children's—Cynthia Meyers and Ben Katz—are really the folks who have been working on that project.

I'll just conclude by saying that I think the research criteria select those in the severe pediatric category. Patients are very impaired and looking at the data, they're a much more homogeneous group. The use of the clinical criteria for those in the moderate or atypical pediatric group who are more variable allows the diagnosis of ME/CFS for those who have the illness but have less severe or atypical symptomatology.

Committee Discussion

Dr. Klimas: How would you propose that we get the pediatric case definition out there both as a teaching tool and as a widely used tool in pediatric practices?

Dr. Jason: One way we've tried to get it out there is by making the instrument freely available so that anybody can use it. We have scoring criteria which we have also put out there. Both the scoring criteria as well as the instruments are available in your handouts. They've also been posted on the IACFS/ME website. Anybody who is interested can freely download these materials.

In terms of how one can get more people to consider these criteria, there are three things that could be done:

- Active efforts by organizations such as CFSAC to make recommendations that other government entities such as the Department of Education make these materials available to their constituents.
- Conferences that focus on pediatric issues, which I think is a much neglected area. We have far less research on pediatric issues. That's another way of getting the commitment of researchers and potentially even funding sources for people who are interested in working in this area.
- Taking questionnaires and publications directly to some of the pediatric organizations and providing information to those groups. Patient groups and scientific organizations could also be vehicles for dissemination.

Dr. Klimas: What's the prevalence of pediatric CFS?

Dr. Jason: There hasn't been a really good study that has looked at this. The Wichita group tried to look at pediatric issues and our group in Chicago has as well. Both of our studies and the Georgia study were focused on adults. We tried to bring in pediatric issues towards the beginning of our study, but it wasn't designed for that. That's still a challenge for the field—to do a really good community-based prevalence study of pediatric ME/CFS. Clearly the prevalence is lower than in adults—at least we think so from our preliminary data in Chicago. It seems to occur more in adolescence, less likely in childhood.

Dr. Glaser: I'll ask this both of Jim and Lenny. If it turns out that these kids or a group of these kids are EBV negative and yet they still have symptoms of CFS, we can start sorting out etiology. Let's say they're negative for both EBV and HHV6 and yet they still have symptoms. Do you have patients like that?

[Question will be addressed during Dr. Oleske's presentation.]

Ms. Artman: We discussed how to get the criteria out there. I remember Anand telling me one time that only the CDC could make an official case definition. Is this something that the CDC can adopt?

Dr. Miller: Lenny has gotten this published and it's in the public domain right now. I don't see why it would not be adopted if it stands the test of time. I was going to ask a question related to this. Have you had any comments from the American Academy of Pediatrics? Would this be an opportunity for a long-term follow up when we have teenagers and young children who are classified as severe?

Dr. Jason: We haven't contacted that group. That's something that is probably worth doing. In terms of long-term natural history studies, they're very important with both adolescents and adults.

Dr. Hartz: I'm impressed with this study. I think you did a lot without even being funded. My impression at this point is that it's better not to have an official definition. As good as this study was, it was very small. There are a lot of things that could be done. Once you have an official definition, it sort of hardens into something that you have to do. You mentioned that this should be the research definition and if you do research, these are the patients that you should study. That's a concern to me because if you only include those patients, then you don't learn what the other options are, where your definition might have problems, and what's going on with the other patients. I think that rather than carving this in stone at this point, it's better to say, "This is a good initial study, let's build on it."

Dr. Jason: I tend to agree with you. I think that one of the limitations that our field has had is that we don't look at the full spectrum of illness, which is extremely important for us to understand. When I mentioned that I think that the severe group could be the research group, I meant that it's nice to have a more homogeneous group when we're trying to look at markers and other types of things. But when we want to understand the full spectrum of the illness, then I definitely think that you would want to have research being done with the clinical manifestations as well as the severe manifestations. I think that full spectrum deserves study, just different types of studies for different issues.

Dr. Oleske made a brief presentation with slides from his patient cohort:

Like Len's study, this was unsupported. I got involved with CFS mainly because I was studying very severe EBV patients and post-EBV people who were having some clear and defined immunodeficiencies. I was involved in a clinical trial to see if IV gammaglobulin helped them. The data I have is on a much more infectious disease-driven group than Dr. Jason's.

What I learned is that besides considering a persistent infection like mononucleosis, there is an important other group of diseases that you need to look at. For example, two of the children whom I've take care of had Behcet's syndrome. I don't think that they would have been correctly diagnosed had they not come for a diagnosis of CF.

There's a whole list of diagnoses that I came across in patients while I was starting to do the work on CF-related EBV.

We did look for differences in T-cells. There was some suggestion in our data of lower natural killer cell activity and suppressive cell dysfunction, but we also saw some monostatic and early cytokine dysfunction.

The dilemma with pediatric CFS is that the patients are symptomatic. Those of us who are doing this should treat the patients as best we can. There can be tremendous improvements in symptoms if you pay attention to pain, allergies, sleep disturbances, etc. A lot of it is working with school systems to provide accommodations. Many times that's an argument that takes a lot of time and effort. You don't get funded to do those things. They become part of the responsibilities.

There are a number of investigational therapies that I don't think we've done much with because we haven't had a clinical trial program where we can enroll patients from multiple sites. The numbers game becomes very important. I can tell you that immunoglobulin helps patients who have subclass deficiency and recurring pulmonary infections, but that may not be the group that we're most interested in.

I think there needs to be some structure put into the care plan with CFS, but that same structured care plan is best carried out by a clinical trial group that enables the numbers of patients to be studied appropriately. Clearly we're talking about a chronic illness model, and that model includes a lot of things I mentioned on the last slide about paying attention to sleep disturbance and other symptoms.

There has to be some reasoned laboratory evaluations. I think there is a list of diagnoses that you can make for your patients. There are some reassurances that I can give based on my experience with pediatric patients that they usually do begin to recover after a period of time, especially those who have a post EBV or CMV (cytomegalovirus) infection or one of the more classically defined chronic viral infectious diseases.

School attendance becomes an important issue. Accommodations at school are mandated by law. It's very important to empower families by supporting them. There are a lot of things you can do to improve the functions and quality of life for children who are going to school, including individualized start times, increased time for exams, home study, and adjusted physical activities. The pediatrician frequently does not know how to address these quality of life issues. Until we come to a better understanding and a diagnostic test, we'll be left with knowing that there are things we can do because of the multi-dimensional nature of these kids' health.

There are a lot of quality of life measurement tools and I think that measuring quality of life should be part of our evaluation, especially for clinical trials. There is a biomedical paradigm for this. Each individual needs to be evaluated independently with the understanding that there's going to be different causations in different patients. We

need to have the groups doing the studies and pulling the data. Besides the physical paradigm, there's the social science paradigm—how kids function, how families deal with that function, and what their roles in society are. It can improve the quality of life to include both psycho-social disease symptoms and physical symptoms.

There's a general assessment for children that I think should be part of the care of kids. Quality of life in HIV was critical when we looked at long-term care. The same thing can be said for patients with CFS. Whatever the treatment decisions, they are going to impact on quality of life, and that's why I think our Quality of Life Subcommittee is so important. Understanding those symptoms, treatments, and social factors are critical. It is amazing how those little things that you do when you don't have all the answers can still make a difference for the child and the family.

Committee Discussion

Dr. Glaser: I have two questions, Jim, and Nancy, if you could also get involved. This is concerning the patients with chronic infectious mononucleosis. Jim Jones told me years ago that in patients like that, if he looks for anti-body to EBNA (Epstein-Barr virus nuclear antigen), they're either antibody negative to EBNA or have very low antibody titers to EBNA. What's your experience in that area?

Dr. Oleske: In children, I would agree with that, that those who go on to have chronic problems do have a different pattern. When you see EBNA come back, there's a tendency for patients to feel better at that time. There is a significant minority population of kids who have what we've been calling CFS that is based on EBV, CMV, or HHV6.

Dr. Klimas: I would ask Jose Montoya, with his serology showing for the patients that improved on anti-viral therapy. That would be very interesting. I don't know the answer.

Dr. Oleske: The other reason why you want to have clinical trial groups is that you keep repositories on these patients. Studies on repositories that have good clinical data are very critical.

Dr. Glaser: My second question: Considering what's going on with the cytokines and the immune system, does anybody know whether the PBLs (peripheral blood lymphocytes) or the macrophages in these kids have NF-kappaB activated?

Dr. Klimas: I have done no kid work on that. Adult work is not very far along.

Dr. Oleske: I've begun looking at some of the functional assays in response to PBL. I don't have enough data, but I could share it with you. I also had analyzed the kids on gammaglobulin. I can't publish this data because when I submitted it, most of the people said, "What are your criteria for diagnosis?" But I can say this: the reason that I think that in a clinical trial network it's important to at least include adolescents is that adults are a much more contaminated population group. Kids who have had chronic

fatigue that has lasted greater than three to six months are a group that isn't confused by all of the other illnesses that adults have.

Dr. Glaser: I agree with that. I hadn't really thought about using pediatric patients as a source, and yet I think they would be a wonderful population to study for the reasons you just said and the discussion we had earlier.

Experiences of Families, Children, and Youth with CFS

Family Perspective

Dr. Lucinda Bateman

As the Education and the Quality of Life Subcommittees met, we decided that we wanted to have a focus on education for the pediatric age group, particularly adolescents and the transition. We thought it would be great to have some testimony from people living through the situation. I've invited Lauren Allen and her mother Peggy Allen to speak to us in person. In order to get a little more testimony, we had three young people including Lauren provide testimony on a DVD.

Lauren is a wonderful young woman who has lived gracefully with CFS since she was 12. We'll let her tell you more about her situation. Her mother Peggy is a professional in her own right. Last year she had an article published entitled *Chronic Fatigue Syndrome: Implications for Women and Their Healthcare Providers During The Childbearing Years*. She also had a review and CME article published in the *Journal of Midwifery and Women's Health* and was awarded the New Author of the Year Award for her work. I'm sure that work comes out of her parenting as much as her professional background.

On the DVD we have three young women who have lived with CFS—Jessica, Jenny, and Lauren. I also want to thank Scot Stevens, who is on the OFFER (Organization for Fatigue and Fibromyalgia Education and Research) Board and has spent time filming and editing this DVD.

Lauren Allen, Utah

Accompanying Document: *Written testimony*

I'd like to preface this speech that I delivered three years ago at a rally for CFS awareness hosted by OFFER in Salt Lake City with an update. Since then, I have graduated from high school with honors and am now enrolled in a local liberal arts college.

My name is Lauren. I am 16 years old. In many ways I am a normal teenager. I worry about the algebra test tomorrow. I can't live without my Ipod. But I'm not like most teens even if I may look like one.

I make it home from my shortened day at school and collapse with exhaustion on the old flowery couch in the basement. On a bad day, I can't make it to school at all. On those days, my glands swell painfully. I have terrible headaches. I lie on that same old couch, willing myself to *move*, to wiggle my toes, open my weighted eyelids. If I can stand, I can barely walk a few steps without my jelly legs giving way to the body they carry. I feel like I just ran a marathon wearing a cement coat. I have CFS.

August 11, 2002. I was only 12 when my life changed forever. I was a competitive soccer player, loved the adrenalin rush of downhill skiing, and was active, social, carefree, *innocent*. I came home from a soccer practice that day feeling a little off. By the next day I felt like I'd been hit by a truck. I'd been sick before, but not like this. I was diagnosed first with strep throat, then mono. But I did not recover as expected. I was too sick to start my first semester of middle school. I had CFS, an illness I'd never even heard of before.

I've been luckier than many with CFS and am so grateful to the many people who have helped me over the past four years. I have been cared for by some bright, caring healthcare providers. I have been supported and encouraged by wonderful, compassionate school counselors, administrators, and teachers. I am sustained by the constant love and care of my family. The help so many have given me has made what could be an unbearable illness easier. If nothing else, I have learned of the beauty in other people, of empathy, of acceptance, of *compassion*.

That's not to say my road has been easy. This illness sucks. The name "chronic fatigue syndrome" does me and others like me a huge disservice. The name is misleading, demeaning, and does not at all reflect the serious, debilitating nature of this illness.

Some experts regard children with CFS as the forgotten population. There's been little research done on CFS in children, and even fewer providers around the country who are educated to care for us. *Please don't forget me* or others like me. I am full of life and potential. I remain a good student. I want to go to college. I want to have a productive career and contribute to our society. I want—always—to have friends and family in my life.

But I need the help of legislators who will promote and vote for funding for CFS research. I need the help of scientists who care and are driven to find the cause and a cure for my illness. I need the help of educated doctors and nurses to provide caring, compassionate treatment that others like me so desperately need. And I need the help of my community to understand and support me like you would care for and support any other neighbor struggling with a chronic, disabling illness. Give me that hope now and give us all this hope for future generations.

And to those of you out there like me, remember the words of author Mary Ann Radmacher: “Courage doesn’t always roar. Sometimes courage is the little voice at the end of the day that says, ‘I’ll try again tomorrow.’”

Committee Discussion

Ms. Artman: You brought up the name and it’s something that repeatedly comes up. We haven’t discussed the name in a very long time and when you said the name, I thought of something: swine flu. The pork industry lobbied and it became H1N1. I just want to look at the CDC and everyone else and go, “Can’t we just give this a number? Can’t I have 467B?” I would much rather have to explain that 467B is a debilitating illness that affects all of these systems. Every patient in this room knows, every doctor in this room knows, CDC knows, that this disease has a societal name that means tired. It’s a huge problem for you, it’s a huge problem for me as a patient, it’s a huge problem for these doctors, and it’s a huge funding issue in the number of grants that get denied because they don’t want to treat tired people.

We got a submission from someone about autism saying that we’re a committee going on vacation to Washington and we don’t do any work. I read this and thought, “It’s our name. We have this horrible name.” Thank you for bringing up the name. I’d really like us individually to look at this and think, “Can’t we do something about this besides CFS?”

Dr. Oleske: I don’t call it chronic fatigue. I call it CFIDS—chronic fatigue immunodeficiency syndrome. Certainly if I have an adolescent with EBV, I think it’s fair to say chronic Epstein-Barr virus infection. You’re absolutely right. CFS trivializes what people have and that’s why we have to fight with the school systems. They don’t understand that when you say chronic fatigue it means that the school has to treat this as a disabling condition. We fight about the name all the time. I’m open for discussion of that. I wish that we did have a different name because I do think that “CFS” trivializes the disease.

Dr. Jason: Rebecca’s point is something that I would second. A number of organizations around the world have been trying to move this debate forward. I hope that our advisory committee can seriously take up the notion. The reality is that everybody experiences fatigue. When you go up to people and you say that you have fatigue, that’s a very common experience. But this particular illness is not what most people experience. That differentiation fails to be understood by far too many people.

Mrs. Peggy Allen, Utah

Accompanying Document: *Written testimony*

August 11, 2002. The day my vibrant 12 year-old daughter Lauren’s life profoundly changed in ways we could have never imagined. Lauren loved and excelled in school, was active, athletic, and easy-going, with a wide circle of friends.

After six weeks of profound fatigue and pallor, stomach pain, severe headaches, and other mystifying symptoms, an astute physician at the University of Utah told us our daughter had a post-infective viral illness and that Lauren met all of the CDC criteria for a diagnosis of CFS except one—being sick for six months or longer. A healthcare provider myself, I was keenly aware that there was something seriously wrong with our daughter’s physical health and I felt desperate for a diagnosis. It is with shame and irony that I admit my initial response to this physician was, “But I thought CFS wasn’t real.”

And so began my own education about the realities of CFS, an “up close and personal” education as I watched its devastating effects of physical suffering, loss, and social isolation in my child and its ripple effect on our family of five. I remember saying to my husband during those despairing early months of our daughter’s illness that I felt like launching a big public education campaign to tell everybody about the realities of CFS. I’m so grateful the CDC and CFIDS Association took on that task.

In many ways, being here today is like a dream come true. I am humbled and honored to speak as a representative for the many other parents and families whose stories go untold.

My daughter was too sick to begin her first year of middle school in the fall of 2002. She missed the first month of school, with frequent and at times prolonged absences thereafter. I remember feeling despaired, wondering how in the world we could manage her schooling considering how sick she was. I remember the pit in my stomach that I would feel at seeing skepticism in the faces of some of the school personnel I would encounter in needing to tell my daughter’s story of profound fatigue that made it impossible for her to sit up for more than a few minutes at a time, caused memory and concentration difficulties, and produced other physical symptoms that added to the difficulty, and at times impossibility, of being in school. It broke my heart to think others were making false assumptions about my still positive, bright, determined, and gracious daughter who wanted nothing more than to be in school and get a good education, and who initially felt too embarrassed to “ask for special favors” as she first regarded the request for 504 plan accommodations in school.

I decided we needed to just tell it like it is, trusting that the earnest and honest person my daughter is would shine through whatever initial false assumptions people would have about her illness, and that perhaps with some education about what CFS is and is not, school officials could help us figure out how we could attain the best possible education for her.

Now, almost seven years later, I’m happy to report that I think my daughter represents a success story. Although still struggling with CFS, she’s adapted, improved somewhat, and with school accommodations has met with academic success to the point of earning a merit-based scholarship for college. Besides her own courage, resilience, adaptability, and dedication to academics, I know her educational success has come from tremendous support from compassionate healthcare providers, school

administrators, counselors, and teachers as well as from the strong advocacy of her parents.

Through a combination of part-time campus learning, online classes, home and hospital schooling, independent learning, and attending school year-round since the seventh grade, my daughter doggedly fulfilled her goal of finishing high school on track with her peers. Her road was by no means easy. She was encouraged by her well-intended middle school counselor to withdraw from the more advanced core classes for which she had qualified. Lauren instead chose to persevere, and with accommodations was able to succeed in these classes.

As a family, we selected a local smaller private high school which, in contrast to our large public high, has a reputation for academic rigor and for fostering a sense of social justice, service, and community among its students. Public high seemed easier, with fewer credits required for graduation. That was not what Lauren wanted. I was referred to the learning disability program coordinator for this private high for consideration of my daughter's admission. I got the distinct impression that this coordinator was either unfamiliar with or had never heard about CFS. I was devastated to hear that the school would not admit my daughter. Rather than give up, I decided that perhaps after some education about CFS, this school would reconsider. After sending the admission committee information about CFS, a copy of my daughter's middle school 504 plan and transcripts reflecting her academic potential, copies of key doctors' letters, including one that served as a disclaimer to any idea that my daughter had some sort of somatoform or mental illness, the school rescinded their initial refusal and accepted her.

Her physician, Dr. Lucinda Bateman, generously went to the school to provide an in-service on CFS in adolescents and related school needs to the principal, teachers, counselors, attendance secretaries, and other interested school personnel. The school principal granted full administrative support to us and our daughter's school counselor to work together in formulating and revising a variety of creative class combinations to help our daughter succeed and remain on campus as much as her CFS would allow. Rather than trying to push her through to graduation without focus on quality education, as is the case with many other students whose stories I've heard, this principal shared his innovative ideas and told her that he'd known other kids with CFS at another school where he's taught who actually excelled in honors and AP classes with appropriate accommodations. He planted this seed of confidence and hope. My daughter was indeed able to succeed in some honors and AP classes by her junior and senior year.

I only wish other students and families struggling with the devastating effects of CFS could be as well supported as we have been.

I suppose one might think that the need for school accommodations for kids with CFS is no different than for others who experience the devastation of other serious illness or disability at such a young age. But please realize the extraordinary challenges kids with CFS and their families face. These students not only suffer from the unpredictable, often times debilitating nature of their illness, but also from the skepticism by which their

illness is regarded. Not only must kids with CFS and their families navigate a healthcare system with few providers educated to diagnose and treat them, they must also try to navigate an educational system with personnel who are frequently uninformed, misinformed, or resistant to providing accommodations to help. Not to mention cost to personal and social development during critical times of growth in a young person with CFS.

Among YPWCFS (young persons with CFS) and their families who have shared their stories with me, age at onset and degree of disability varies, but a common thread in experience is the parents' perception of needing to "fight" for their child to receive a good education, or in some cases, for parent or student to feel so dispirited by a lack of understanding and support that they give up trying. Parents' struggles with the school system are all the more complicated if there is a delay in CFS diagnosis for their child or if the family is not aware that CFS disability can qualify the child for legally protected accommodations for an equal education. Children with CFS are often times in a difficult bind. Pediatricians who are more experienced dealing with the school system on behalf of children with other chronic illness are vastly unfamiliar with CFS. Physicians who specialize in CFS typically do not treat many children, so may be unfamiliar with ways they can help their pediatric patients with school needs.

I've been told that despite being on a 504 plan in school, a bright student with CFS who performed at an A level through assignments and test scores in two of his high school classes was given failing grades by teachers due to point deductions from absences. After an appeal by his parent and school counselor, one teacher reluctantly compromised to a B minus; the other refused. This parent feels strongly that many of her child's teachers doubt the reality of his illness and regard his 504 plan as preferential treatment which biased his grade. The waxing and waning nature of her son's illness was misunderstood. Like many others, he is capable of accomplishing great things in school, but on some days he cannot accomplish much of anything at all.

Several other parents felt that the school basically gave up on their child. They told stories of feeling like they were doubted and left to flounder in trying to figure out ways their child could obtain a good education, knowing their child still had the will and potential for academic success despite the challenges they faced with illness. Rather than trying to problem solve to meet educational goals, the school pushed their child through to high school graduation by enrolling them in classes below their scholastic abilities. This was easier for the school, but cost the child a good education. Some even told stories of feeling like they or their child were dealt with in a demeaning and disrespectful way by unsupportive teachers and attendance secretaries.

The few families who were aware that medically documented disability with CFS could qualify their student for college board accommodations and for vocational rehabilitation benefits discovered this on their own, not from school counselors. A couple of students abandoned plans for college, as tuition costs seemed prohibitive considering the students' inability to work while attending school and anticipated inability to be healthy

enough after graduation to work fulltime to repay student loans. The lack of education and support by our school system of YPWCFS is a travesty that adds to their suffering.

As described to me by a former special education administrator and mother of a 24 year-old daughter sick with CFS since age 10, it is “inconvenient” for school administrations to devise an individualized educational plan that can work for a child with CFS. As she describes, CFS doesn’t fit neatly into the established categories of illness or disability that legally qualify kids for school accommodations. In reference to creating an educational plan that can work for kids with CFS she says, “It doesn’t have to take more money—just caring hearts, open minds, and better planning.”

To those involved with the educational system, I urge you not to give up on children with CFS. They desperately need your help. Realize that the vast majority of these children value quality in education and long for a healthy life that would allow regular school attendance. Recognize that the academic potential that existed before the onset of illness can still be nurtured and developed with your support, compassion, creativity, and flexibility with a true team spirit in working with the student, their parents, and their healthcare provider.

The level of support you provide can make or break a child with CFS’s ability to succeed in school, with lifelong impact on self-identity, worth, sense of accomplishment, and level of ability to function as an independent adult. The investment of your time, interest, creative efforts, and compassion are invaluable to improving the quality of life of children with CFS and their families. As I sit here with my daughter with CFS who is about to begin her sophomore year in college, I can attest to the fact that your efforts will be well worth it.

Thank you.

Committee Discussion

Dr. Hartz: If you could recommend changes that would affect broad number of school systems, what would you recommend could be done to help the school system or other kinds of civic organizations so that each time this came up it wouldn’t have to be another parent struggling with the whole process?

Mrs. Allen: I don’t think there’s a quick, easy answer or solution. I think that it would need to be multi-faceted. Better education for the American Academy of Pediatrics for pediatricians in general practice about what CFS is and how it affects a student’s ability to function in school would help. Most definitely, education of school nurses and society in general about the realities of CFS would help. School counselors are not in tune with sources of support that are available to children with CFS, especially as they prepare for ACT exams. Educating counselors that children with CFS qualify for those accommodations and can apply for vocational rehabilitation benefits for college funding would be very helpful.

Dr. Hartz: Is there any way that CFS education for school officials could be part of a larger program that these people receive?

Dr. Oleske: I've had a lot of experience. There are two issues. One is that there's a lot of autonomy in school systems. The local school systems have certain guidelines that they have to follow from the state but there can be major differences across areas. A lot of times the local school system will be a real negative. You have to spend the time writing the letters and going to the school boards. That's critical. If you don't have a pediatrician or specialist advocating directly to the school system, it's very hard for families to describe and argue for their child. You see those tragedies of children who could have succeeded but haven't succeeded.

The other issue is having the family unified on this. CFS sometimes splits families where one of the two parents is sympathetic and the other one isn't. I spent a lot of time talking to the parent who was very negative about what was going on. The problem is that it's not an acute enough symptomatic disease. People say, "look at your daughter. She looks perfectly healthy."

Dr. Jones noted that the Department of Education would be appearing before CFSAC and encouraged committee members to identify some ways to be helpful.

Dr. Papernik: What would the proper approach be? Fan out and educate educators? School systems? Counselors? School boards? Or is the approach better served educating the pediatricians about what CFS is and how to go about getting the school accommodations that these kids need? I treat adults, but once in a while I'll have an adolescent come in. All I do is write a letter to the school saying, "She needs accommodation." I would like to know more about adolescent accommodations that really need to be fought for on behalf of the children who need them. I think that might be an area where we're lacking—getting the pediatricians to recognize that this is available for these kids.

Ms. Artman: Both the Education and the Patient Care/Quality of Life Subcommittees are moving forward on inviting the National Association of School Nurses to appear before CFSAC.

Dr. Jones noted that the day's agenda marks the first time a representative from the Department of Education has appeared before CFSAC. She added that the day's discussions were not meant to immediately solve problems but to shed light on the linkages between the Education Department and outreach and begin to set up an agenda that CFSAC can pursue in subsequent meetings and subcommittee activities.

Dr. Glaser: People respect information when it comes from the CDC. The agency could play an important role in interacting with the school systems. If information comes from the CDC, it should help school officials listen.

Youth Living with CFS

CFSAC viewed the video “Youth Living with CFS.”

Committee Discussion

Dr. Oleske: I could not agree more with the accommodations issue. Unfortunately we do have to go state by state and in some states, you have to go county by county. That’s a long battle. I don’t know if the CDC could change things. They did that for AIDS. There were a lot of issues about AIDS and kids not going to school. The CDC was active in that campaign.

Dr. Miller: We actually do have a Division of School Health which could play a very important role here. Should I take this idea to them? I don’t know that they’ve heard it before. They may ask if there’s a toolkit available. What can they do to get this information out? There has to be a place to start. I’d like the Division of School Health to have that DVD.

Dr. Bateman: Our nonprofit will make that DVD available to anyone who thinks it would be useful, whether it be school counselors, school nurses, or a division of the CDC.

Dr. Oleske: There has been a marked cutback on school nurses. That is a terrible disservice to communities. There is some talk about reestablishing the role of school nurses. The other issue is the tremendous independence of local school systems to even make decisions contrary to state policy. With AIDS, we joined forces with the CDC and states and they eventually allowed kids with AIDS to go to school. What we’re talking about now is a different issue, but it’s the same general point—how do you reach out to these independent, very locally controlled school boards?

Dr. Jason: Literally thousands of kids out there don’t have parents who understand what’s going on with them and physicians with the proper training. The effort that needs to occur is monumental. Where do you start? We need a resource center that can get information out. We need training for all the different groups we’ve been talking about—the children and families, school nurses, and physicians. One thing is not going to work for everybody. This is a complex problem and it won’t get solved unless resources are available.

Dr. Snell: Mrs. Allen, Lauren, did you look into the public school? Did they have accommodations that were available?

Lauren: They did, but academically it was no where near on par. We did find that once we were accepted into the community of the private school, the support was really unparalleled in individualized attention and caring for me being there and making me feel valued—the things that a lot of kids have expressed was absent in the public school system with a lot larger classes. They did have a disability center that we were referred to and we talked to that person before deciding to go to the private high school.

Mrs. Allen: Our public school is quite large and it would have been physically hard for Lauren to walk through the building from class to class. We also knew a family that had a very negative experience with a daughter with CFS who went to that public high school.

Dr. Snell: Did the private high school give a reason for the first rejection?

Mrs. Allen: The learning disability coordinator said that they could not accommodate her need to be in school part time. I do believe that it was also from a lack of understanding of her illness initially, but eventually they were totally on board and very supportive.

Dr. Snell: That's also an issue, because a lot of school districts are opting to go to charter schools, which get state funding but are also able to exclude students based on certain criteria. In the interest of keeping test scores up and looking good, they try to exclude students who they think are going to be problematic in terms of achievement.

Dr. Bateman: Hardly ever do my patients go to a private school, because there just aren't that many private school opportunities in Salt Lake. My experience has been that even in a community where we have a huge amount of education for providers and there's a lot of awareness, the school districts are pretty disinterested for the most part. They don't like students coming part time, they're uncomfortable with students not having enough credits, and there are not a lot of options for students to make up those credits. Many students just end up on home hospital, which means that once a week a teacher will come by for two hours. That's about the extent of what they get through the school district.

Lauren: Just to clarify, I did go to a public middle school for two years. They did work with us there.

Parent Perspective

Rita Driscoll, New Jersey

Accompanying Document: *Family Perspective on CFS*

This conversation for the past hour is very upsetting to me.

Thank you Dr. Wanda Jones. My name is Rita Driscoll. I am the mother of three children. My oldest son, Johnny, just turned 26 years old. My daughter Elizabeth is 24 years old and my son Frankie is 14 years old. Ironically, Frankie's birthday falls on Veterans Day, November 11. My father, Raymond J. O'Neill, who served on the USSO Savo Island in the Pacific and Frankie's late grandfather, Frank S. Driscoll, who was awarded a Purple Heart in Iwo Jima, have given my son Frankie a great admiration and respect for our country's government, which plays such an important part in what I am here to talk about today.

To give you a better understanding of families with CFS, let me tell you about my own. I am one of eight and my husband is one of 14. My children and I grew up with a great support system, which included 40 cousins. Now, imagine my families' reaction when I told them this story:

In March 2007, we had just returned home from the hospital with Frankie after another draining and disappointing visit that left me with nothing more than I had started with. The doorbell rang, the dogs barked, the rain was pouring down, and my body was aching. I opened the door and my whole family's lives changed. There stood Ms. Ricks from the Division of Youth and Family Services, DYFS. She told me there had been a complaint against my husband and me for neglect and abuse on Francis. I kept my composure so that my son Frankie would not be afraid, but more importantly, so that he would not be disappointed in a system that he so greatly admired, which is the government.

Ms. Ricks conducted herself like a professional as she was trained. I have much respect for what she does. However, this visit from DYFS would not be the last. Upon the second unannounced visit, to which Ms. Ricks was not a part of, two nurses entered my home and questioned Frankie on CFS. "And by the way, what is mono Frankie?" They took his blood pressure and weighed him. The entire time these nurses were in my home, Frankie's friends that day were invited over. They asked Frankie, "Who are these people?" Frankie said, "They're nurses. They're just taking my blood pressure."

After that he said, "Mom, no more." I said, "No one will come here and speak to you or me. I probably will have to get a lawyer and find out what our rights are." But I continued to cooperate with Ms. Ricks. There was nothing that I wanted more than to educate the person that accused my husband and me of abuse, neglect, and the second charge, Munchausen by proxy.

I have to tell you a little bit about Frankie. In 2001, a rheumatologist in my town gave him a diagnosis of CF, FM, arthralgia, and question mark myalgic encephalomyelitis. I said, "This is great. Now we have some sort of a diagnosis." He's eight years old. By the time Frankie was 12, he had seen two pediatricians, three neurologists, two cardiologists, three gastroenterologists, two metabolic specialists, two oncologists, two hematologists, two rheumatologists, two orthopedics, one neurosurgeon, and two infectious disease specialists. He had undergone one colonoscopy and two endoscopies. He stayed in the hospital overnight on three occasions and had at least 15 ER (emergency room) visits. Not to mention his week-long stay at the Mayo Clinic. What I feel is important to mention is that after all of this, the government came into my home, asking my family questions, wasting our time, money, and making something already so hard to cope with so much harder.

What stress does to a family; what illness does to a family. We missed out on vacations, parent weekends, sports games, and countless experiences that children deserve to go to. When friends were swimming in pools, walking into town, seeing the latest movie, Frankie was on the couch asking me to carry him to bed. Listen carefully,

because this is so upsetting when a child goes through this. A regular night included chills, fevers, vomiting, insomnia, and diarrhea. I would get a hot bath ready, put his blankets in the dryer to make them warm, and worry whether or not my husband and I would have to take him to the ER. When I would tell Frankie it was necessary he would say, "Please Mom, don't. I hate that place. Just tell me funny stories." The hardest part about those nights was convincing a little boy—a male, not a female—that he was not going to die and reassuring him that we would get the answers.

I could talk for hours about the countless nights I spent with Frankie and the emotional and physical pain that has occurred, but believe it or not, my biggest battle has been to get an education for my son. Because of the nature of ME/CFS that hides on good days and pops out to scare you on bad, not one school official, teacher, or counselor believed him. I printed out handouts on CFS just to be given them back and have them thrown in my face. They would say, "Sorry we can't teach him if he's not in school." The head of special services said we needed a better diagnosis. It was heart-wrenching to think of all the specialists I had visited and all the doctors' notes I had provided without receiving even the slightest bit of compassion. There is no excuse for discriminating against a child so young with such a debilitating disease.

I have so much information on Frankie that I will and would love to share with all of you doctors and the CDC, because where I come from, Bergen County, NJ, the teachers were all educated. They had four-day conferences to learn about CF. They laughed. They didn't allow Frankie an elevator pass. They didn't allow him to have water when he asked. There's no excuse for that behavior whatsoever. When I found the 1995 CFIDS explanation of the disease I said, "OK, we're at 2009 and it seems like we're still at the same standstill." We need funding, Congress, for chronically ill children. You cannot ignore these kids because by the time they become adolescents, if they're ignored, they will find something for that pain. The biggest problem Frankie had was trying to find some sort of temporary pain relief. The pain hurt so bad, he felt like he was going to die.

I could add IEP schedules that have been made up for Frankie since first grade. For four years, on his report card, he got M for medical. Who taught him? His IEP 504 classifies him as health-impaired. I believe that the state gives money to that school for that health-impaired child. So I read some rules, I went to the school with a bit of an Irish temper, and I finally got what I had asked for way, way in the beginning. I needed Frankie to go to school part time. I needed a tutor for him to go the library so he could be out in the public. And I needed the school to agree to ten hours of tutoring at the library so that Frankie could go into school whenever possible, because he loved school. There's not one teacher throughout his twelve years of schooling who didn't say he was a joy. He would go into class after missing three weeks and just continue.

He was not provided computers. He was not provided Microsoft, although it's written in his IEP. He wasn't provided anything. He taught himself an awful lot. And my family and the support of so many in my family helped Frankie get better. And when I say get better I mean that in the last year he has stayed at home resting, eating good, and

having a schedule and a compassionate tutor, who has saved his life and who has made Frankie again a very energetic, positive learner.

I had a meeting with the IEP team for school as Frankie transitions into high school. There is no plan for Frankie. They want him to be in all resource classes. Even though his IQ is high, his fluency rate is 6 percent. His cognitive ability to do math diminished after a very high fever in 2001. And I'm going to end this because I don't know if I'm getting through to any of you, but the state of New Jersey dropped the charges of neglect. It was unfounded after three months of contacting every one of my doctors and Frankie's. The doctors were appalled not only that somebody would be so vicious but that they had to spend time filling out two pages of questions. We're asking doctors who are seeing 20-40 patients a day to all of a sudden stop.

When the Mayo Clinic sent correspondence, the school finally kind of opened their eyes and said, "Now we'll listen a little bit" even though I had many doctor's notes from very reputable places. The letter states, "Our final diagnosis: CF, musculoskeletal discomfort, abdominal discomfort, mild dysautonomia, circadian rhythm sleep disorder, history of anemia, mild neutropenia, and left ventricle hypertrophic on an EKG." While I guess a parent would be happy with this—Frankie was thrilled because all he could hear was a word called "mild" dysautonomia. When we say mild dysautonomia, what I had to explain to people was it was a dysfunction of the autonomic system, which includes brain, heart, and stomach. They would say, "Everything else is OK, right?"

Frankie at some point in the last eight years was so white, so underweight, it was heart-breaking for the whole family, and yet there was always this distant hope, especially speaking with my father, who used to say, "Dear, don't worry. Let him rest. I used to have the fever and chills always as a kid. But I went to the Navy, and look at me now. I'm 85 years old." It was a positive attitude. But the more negativism that we give to these children as they grow up, we're going to have a bigger problem. What is written about Frankie in all the IEPs that have been written about him has wasted many, many thousands of dollars of our good hard-earned taxpayer money.

I beg of you, the CDC, you have enough information. You need to make the public aware just like you did with the swine flu. When Frankie had a temperature of 104, the pains in his head were just killing him. If I went to the hospital, they probably would have done a spinal tap. No way. Then they wanted to do a muscle biopsy. For what? Then bone marrow aspiration. He went through all of this, not to mention a very rare metabolic disease. Your criteria, from what doctors and teachers have told me, is criteria for exclusion, meaning if you're going to give Francis Driscoll a diagnosis of CF, then you have to exclude all these other diseases.

I would agree too. But there are big problems with our labs. Frankie would take blood one day and his white blood count would be three. Two days later, it was 15, 18. Another day later the doctor would say, "Let's do another one. Let's see if it's the labs." All the labs were different. Frankie's blood was sticky; it was diamond-shaped. I heard

so much that I said, “Let’s send the blood to the Mayo Clinic or to a clinic that does specific testing for this.”

I know that all of Frankie’s levels are low, and they may have been from birth. When I gave birth to Frankie, I had a temperature of 103 and I stayed in the hospital for five days. They never told me what I had. I knew what I had. It was just another fever with chills because I overexerted my body with 25 hours in labor. And that occurred with all three of my children.

If we went back to Frankie’s records, at two years old he had a severe staph infection. And from there he had very unusual infections, not your typical ear/nose. It was viral. Can we talk about the EBV virus? Twice he’s had the EBV virus. He’s also had the parvovirus. When I was in the hospital with Frankie asking for IVIG (intravenous immunoglobulin) a wonderful immunologist came in and said, “Oh no. His parvo titers are very high and I don’t want to be that little percent that gives Frankie IVIG with parvo in it.” Wow, how much knowledge do I have about this? By that time, quite a bit. I thanked the immunologist and he said, “I have to find something for this kid. I have to find something.”

The Mayo Clinic believes that Frankie’s immune function was compromised by the EBV. I welcome anybody to take his records. You can make a template out of Frankie Driscoll because in 2001, a neurologist gave him the diagnosis of myalgia. Frankie couldn’t grab a pencil and he couldn’t add after that fever. And from there on, his fatigue and his infections got worse and worse until he could no longer even walk up the stairs.

It is your job, CDC, to educate the teachers, the caregivers, the professors, the universities. The swine flu didn’t cause all of us running to the emergency room, but mothers have to be aware of what high fevers can do to a child; to a young baby. High fevers and head pain—myalgic encephalomyelitis—could we use a bigger word for these children? But you cannot say “chronic fatigue” to Frankie. He won’t accept it. So I ask you Congress to please send some money over to the CDC so you can make some more public awareness messages to get through to the whole United States so my son is no longer discriminated against in his community, by his teachers, by his peers, by everybody.

Frankie’s doing great. He’s got a wonderful, wonderful attitude. I thank you so much for all the work that you’ve been doing, but I think we need to get on with it.

Committee Discussion

Ms. Artman: You talked about temporary pain relief. What did you find when he was in school was the biggest way to alleviate his pain in the classroom? I’ve heard pillows, I’ve heard blankets. What are a few fixes that you see that would tangibly improve the lives of every CFS child in school?

Ms. Driscoll: Every child's nervous system is different. Two milligrams of Valium made Frankie hyper and his legs feel shaky. The first issue that needs to be addressed is the sleep issue for children. When he went to the neurologist at the Mayo Clinic he said, "I'm just dying for a good night's sleep, please." That is the hardest because when you don't sleep, your pain is worse.

What works for his stomach after so many times of throwing up is Zofran to stop the nausea. Donatal helps the cramping in Frankie's stomach. Pain relief is temporary for these kids and I believe they don't want to take a pill if it's not defined what they really have.

We tried melatonin and that started to work until a strep infection caused the cycle to become worse. If somebody here can decide on a good sleep medication for a child, that would be a wonderful start. Next would be temporary pain relief that I can give to Frankie and say, "It won't affect you later on in life." He wanted to know about Lyrica because of the FM ads on television. So much of this is female related. For a young boy growing up having this and having a stigma attached to it as if it is just a female disease, that's a frustrating feeling. Lyrica at 25 milligrams stopped the pain, but he felt foggy, so he couldn't go to school. But I also found that Frankie didn't have to take Lyrica every day. When he felt that burning pain in his legs—the feeling of that chronic fatigue coming on—I would know then that I could give him Lyrica and it would make his pain from 10 down to five, which was great for Frankie.

The neuron tryptamines made him shake. Muscle relaxers for his stomach gave him diarrhea. Treating the symptoms as they come is the most important thing for a child. Medically we have an awful lot out there that has been proven to be safe. Doctors need to trust the mothers and the patients and listen to the patient. Even though Frankie was only eight and now 14, he could have a wonderful discussion with all of you about what it feels like to go through what he's going through.

Dr. Jones noted that the role of CFSAC is not to determine drug efficacy or to make recommendations or endorsements and that Ms. Driscoll was relating her personal experiences.

Dr. Klimas: Dr. Kathy Rowe from southern Australia described at our last meeting her highly successful program for adolescents, which created interaction among healthcare providers, the school system, and social services. Your story about Munchausen's was chilling. Unfortunately I've heard much, much worse stories and have cared for patients with devastating family encounters with the system. I'm so glad the Department of Education and others are here.

Dr. Miller's offer to work in CDC with the school health program is extraordinary, but he asked for a toolkit and we need to do that in some way. We're not really the committee that would, but we have the experts here or access to the experts who could. I would ask that we not let that drop. If Dr. Miller would put me in touch as a citizen with someone in his school health group, I would challenge Pat Fero, Kim McCleary, the

IACFS, and interested parents to come together and have an open discourse to try to develop a toolkit. It would be very cool to come back to the committee in six months with a toolkit in place that could help children.

Dr. Bateman: We on-purpose tried to show the extremes of children who are well-resourced with that combination of family support, well-educated medical provider, and a connection with the school system that was willing to make adjustments. You can see when those things are missing that everything comes to a standstill despite the enthusiasm and support of the family.

Dr. Oleske: I think that we could develop a kit, because we already repeat the same thing each time with each school board. I would caution you that underserved children in families that do not have the resources that some of the families have here also need to be considered. The options they have are much more limited. If we do develop a toolkit, it should be able to be applied in all areas for underserved as well as served children.

Ms. Healy: We need to remember that in addition to the community health centers, which are Federally funded, there are also numbers of school health clinics that are also publicly funded. If we want the Federal pipeline to include more provider education, I think that might be a place to direct some of our efforts.

Dr. Oleske: School nurses, although critically important, have been cut. Now, with Obama's plan, I think there is a sense that there's going to be a reintroduction to taking advantage of the school system. They could have a very positive impact on the disease if they have the right training.

Dr. Bateman: There's nothing like the authority of a physician to make things happen for the patient. That's why this absence of primary care support in pediatrics for patients with CFS is just a travesty. The Federal and state resources are much more likely to be provided with a letter from a doctor or anything that conveys authority.

Ms. Driscoll: I had the letters. It took me five years to get to where I am now. That boy was left alone for five years. I had the resources, I had the diagnosis, the teachers and counselors knew.

Mr. Newfield: Where was the flaw? Where was the gap?

Ms. Driscoll: The special education learning services that take care of the children with 504s and IEPs (individual education plans). I thought that Frankie's disability was always under health impaired. No, he was under learning disability. Under health impaired you get more, although he didn't get certain things that he should have gotten even under learning disability. It's the individual school. The Mayo Clinic gave them handouts. I had been giving them handouts since third grade. They didn't take it seriously. They never saw Frankie the way my family saw him. He only went to school when he felt strong. There's a difference between a boy and a girl with this disease.

They both suffer, but a boy is not going to go into school when his bones are aching because guys at that age, they like to wrestle. It starts from the school administrator, which I would say is the principal. DYFS calls the school to get the low-down on the child. There has to be better communication between education and DYFS.

It's not hard to teach a child who wants to learn. And even if they're sick, they can lie there and listen. Their ears are open, and that's how Frankie learned.

Dr. Oleske: Part of the problem is that the services for disabled children usually deal with the child who has some severe learning disability or a child with multiple handicaps. When school officials see a child who is able to function at times, they make the assumption that the child can do that all the time. That's where the education has to be. You can have someone who doesn't look sick and who isn't in a wheelchair who at times is unable to participate in the school system. That's very difficult for them to understand.

Dr. Jason: Michael's offer is extremely valuable. I think that we should also think about the power we have as an advisory committee. This is a crisis. Another way for us to think about this is our ability to bring critical stakeholders together to really think about how we can address this issue in a comprehensive way.

Roundtable Presentation/Discussion

Dr. Jones expressed her gratitude that roundtable presenters arrived early in order to see the morning's presentations and DVD. The afternoon's presentations and discussions would be richer for the context gained, she said.

Child Protection Programs

Catherine Nolan, Director, *Office of Child Abuse and Neglect, Administration for Children and Families, HHS*

Accompanying Documents: *The View From the Children's Bureau; Child Welfare Information Gateway folder*

In listening to the previous discussion, I think that my role is probably pretty minimal. Wanda was very interested in my coming to meet with you today just to inform you about the fact that we do have a Children's Bureau within the Administration for Children and Families and within that bureau is my office, the Office of Child Abuse and Neglect.

My role is to give you some examples of the information that is available through our Child Welfare Information Gateway. [Ms. Nolan directed CFSAC members to material provided in the Information Gateway folder including a fact sheet describing the history, purpose, and processes of the Children's Bureau; a fact sheet on its programs; and a bibliography of articles on CFS in children from 1998-2009. The purpose of the

bibliography was to demonstrate how her office staff can search the gateway library for requested topics from CFSAC members.]

The Administration for Children and Families is directly beneath the HHS Secretary's Office on the organizational chart in a sublevel cabinet position. We do not have an Assistant Secretary yet. All of the programs that have to do with children and families fall under the Administration for Children and Families.

History

- The Children's Bureau is the oldest Federal Agency dedicated solely to the welfare and well-being of children. We were created in 1912 by Executive Order by President Taft. The issues that the bureau dealt with in those first couple of years were infant mortality, birth rates, orphanages, juvenile courts, and child labor laws.
- The bureau was initially housed in the Department of Labor before being moved to the old Department of Health, Education, and Welfare and then HHS.
- In 2009, any of Federal legislation that has to do with child welfare comes to the Children's Bureau for implementation.

Mission: The Children's Bureau seeks to provide for the safety, permanency, and well being of children through leadership, support for necessary services, and productive partnerships with states, tribes, and communities. Safety, permanency, and well being—those three phrases are the real drivers of the work that we do.

Relevant websites:

<http://www.acf.hhs.gov/programs/cb/>
<http://www.childwelfare.gov/>

[Ms. Nolan described the organizational chart of the Children's Bureau, highlighting the Office of Child Abuse and Neglect.]

The Children's Bureau has an annual budget of \$7.5 billion. We work with state and local agencies to develop programs that cover the spectrum of child welfare from prevention of child abuse and neglect to finding placement for those who cannot safely return to their homes.

Scope of the Problem

- The gateway folder contains the executive summary of our 2007 annual report. These reports are issued each April during Child Abuse Prevention Month.

- In 2007, there were approximately 749,000 substantiated cases of child abuse and neglect. Those are the cases that have come to the attention of the Child Protective Services agency.
- On any given day, there are approximately 500,000 children in foster care in the United States.
- 130,000 children are waiting to be adopted from the foster care system.

In 1996, the Child Abuse Prevention and Treatment Act (CAPTA) reauthorization created the Office of Child Abuse and Neglect within the Children's Bureau. It was reauthorized again in 2003. Under CAPTA the office:

- Provides leadership and direction on child abuse and neglect prevention and treatment.
- Serves as the focal point in intra/interagency collaboration.
- Leads national conferences and special initiatives.
- Coordinates prevention activities, particularly through Title II of CAPTA. The community-based child abuse prevention (CBCAP) program is a formula grant to states. We operate that program out of my office.
- Supports systems improvement through the Children's Justice Act (CJA). We receive \$17 million each year from the Department of Justice. CJA language is very specific as to what the money can be used for: reducing child trauma, particularly in child sex abuse cases; improving the handling of child abuse prosecutions; and improving the handling of abuse-related fatalities.

The Spectrum of Child Welfare (the range of the case)

- Protect children from having to come into care in the first place through prevention of child abuse and neglect.
- Provide child protective services.

These are the two main focuses of my office. Other divisions within the Children's Bureau focus on:

- Family preservation and support.
- Foster care and kinship care.
- Adoption.
- Independent living/transition services for youth.
- Working with the courts – we have a court improvement project.
- Interagency collaboration.

Child welfare is primarily a state responsibility.

- At the Federal level, Congress enacts the legislation; then it comes over to us.
- We at the Children's Bureau are implementers of the legislation by providing monitoring and oversight. CAPTA is under our purview. We make sure that

states know about all the provisions. There is money that they can apply for. They don't have to apply but if they do, there are certain assurances that the governor must make.

- The states do establish the child protection programs and most have their own state statutes.

Primary Legislation of Interest

Child Welfare Services Title IV-B, Subparts 1 and 2
CAPTA

- CBCAP - \$42.5 million
- CJA - \$17 million
- Discretionary grant funds - \$39 million. These grants give us the flexibility to really move the field along. We use the money to carry out requirements within the legislation. The laws also have a laundry list of research and demonstration projects that they would like us to look at. We couldn't possibly fund all of it, but every year we go through the list, come up with ideas, and issue competitive grant announcements every spring. The idea is to develop the body of knowledge through research and best practices through these demonstration experiments. Projects have included:
 - quality improvement centers
 - substance exposed newborns
 - evidence based and home nurse visitation
 - comprehensive assessments to improve child welfare outcomes
 - National Resource Centers
 - Child Welfare Information Gateway

The bulk of the \$7.5 billion budget goes out to states for their foster care and adoption payments. The bureau has the responsibility to monitor what the states are doing with that money via the **Child and Family Services Review (CFSR)**:

- We oversee state performance related to child welfare outcomes and systemic factors.
- The states conduct their own self-assessment.
- We provide them a state child welfare data profile.
- A team goes onsite to conduct a random review of 65 records including interviewing all of the people involved in the cases.
- We conduct interviews with stakeholders.

All of the instruments that the teams use are on the website.

This system was mandated by Congress and combines a qualitative review with a quantitative review:

- We have national standards that were created based on the data. The evaluation measures state conformity with these national standards.
- We think that it's a good thing to have data-based outcome measures.
- Safety, permanency, and well being for all children constitute the three outcomes. Under each outcome are systemic factors and case level indicators that all feed into those three outcomes.
- We completed the first round of reviews of all 50 states, the District of Columbia, and Puerto Rico in 2005.
- We began our second round in spring of 2007.

General review findings:

<http://www.acf.HHS.gov/programs/cb/cwmonitoring/results/genfindings04/genfindings04.pdf>

PowerPoint:

<http://www.acf.HHS.gov/programs/cb/cwmonitoring/results/statefindings.ppt>

A large part of what we do is providing information and training and technical assistance resources to states and tribes. We've been working hard in the last several years to develop a sophisticated network of more than 25 Network members through:

- National Child Welfare Resource Centers
- Quality Improvement Centers
- Implementation Centers – a new project started in 2009. There are currently five centers designed to work with each state to hone in on issues that came up in the CFSR or examine a part of the system in which the state wants to make in-depth improvements. The center will work one to two years with the state.
- Intra-agency agreements - My office has a strong mandate for interagency coordination and collaboration. I chair a Federal interagency work group on child abuse and neglect.

Other joint projects:

- National Center on Substance and Child Welfare - co-funded with the Substance Abuse and Mental Health Services Administration's (SAMHSA) Center for Substance Abuse Treatment.
- Participation in SAMHSA's National TA Center for Children's Mental Health.
- TA Partnership for Child and Family Mental Health with SAMHSA.

Connecting with CFSAC Concerns

- The dissemination arm of the Children's Bureau in my office really is the Child Welfare Information Gateway, which puts out an electronic monthly newsletter, *Children's Bureau Express*. If someone from CFSAC wanted to write a small article to contribute, we could consider that for the gateway.

- You could submit information to be included on our web page under hot items/what's new. The website is where we do the vast majority of our communicating.
- We have a searchable database that's phenomenal, with information specialists who can be called for assistance. I was impressed that they already had such a huge bibliography on CFS in children.
- We also have many, many listservs of all of our various constituencies such as grantee groups and the state liaison officer (SLO) in each state designated to interact with the bureau.
- The National Resource Center on Child Protective Services convenes the SLOs once a year and has a newsletter that it sends out to the SLOs.
- We issue annual prevention packets every April during prevention month.
- We host a national conference (the next to take place in Washington, DC, in 2012). The call for papers usually generates about 500 abstracts. The conference includes workshops and an exhibit area. The next conference will take place on the 100th anniversary of the Children's Bureau, so we're making a big deal about it, including holding events throughout the year.

Committee Discussion

Dr. Glaser: Can you give some examples based on the CFS families' stories of how you could have helped them?

Ms. Nolan: To me, this is incredibly complex. I think that there are a couple of challenges:

It's the states' jurisdiction. We issue the general guidelines; then it's up to the states to work within those general guidelines to determine what their state child welfare system is going to look like. Our role is to provide technical assistance to the states. In many cases, the child welfare system is county-run. Penalties can be assessed if states don't meet their benchmarks.

I have listened for 11 years to feedback from CPS agencies and well as from the public. We probably get just as many letters and emails from the public saying, "Stay out of my hair. Why are you sending people to my house?" as we do saying, "Where the heck were you? This child died. Why weren't you on the watch?" **In this country there's consensus that children should be safe but how that should happen is very contentious.**

Dr. Glaser: I understand the sensitivities of territoriality, but it seems to me that it's possible to sensitize the other players within the states that these are issues out there. That would be a helpful thing to do and still stay within your territory.

Ms. Nolan: That's why I mentioned the different venues where that might happen. That SLO network that we have—those folks are all in a position to influence the training that goes on in their states and communities. We need to hear from the

medical research community. Every child presents with different needs, which we understand, but solid the data that the medical research community can provide to support the work is always helpful.

Dr. Glaser: That's why the CDC is so important. There's your resource.

Dr. Oleske: We always say that children come first, but in the application, that sometimes doesn't happen. In my experiences, children with chronic illnesses do not get services, especially if the disease doesn't have a name like cystic fibrosis, where there are a large number of patients. What I have found in working with children with AIDS and CFS is that if we were to approach the needs of children based on having a chronic condition that sets up multiple roadblocks and problems for the family and accept that we will now provide services that look at providing good palliative care to patients, I think we can address a number of conditions like CFS or autism.

Children with chronic illnesses will survive their parents. I'm really concerned about the housing of children who are chronically ill when their family is no longer able to help them. While it's not directly applicable to children with CFS, I think there are times when that is going to be an important issue. I think that the Children's Bureau is starting to address that. In that context, how can we help children with CFS by looking at these long-term issues?

Ms. Nolan: That's a great question, and a personal one. I have a brother who has a daughter who has Downs syndrome and all the related medical complications. That is a personal worry of mine—what will happen when my brother can no longer take care of her. I think I have a big enough family that we will take care of her.

The only correlation in terms of the Children's Bureau is the issue of children aging out of foster care. A way to think about it is that we "raised" them and they leave home at 18, but are they really ready to leave home at 18? That's what the Chaffee legislation was all about—the independent living program and the educational vouchers. It was a very responsible thing for Congress to do because it gives that cushion of a few more years after the children age out of care. I'm not aware of anything that we're doing specifically at the Children's Bureau around the much longer term issue that you're talking about. I don't know if other agencies are thinking about that.

Dr. Oleske: There really is a frustration among citizens that we have wonderful institutions like the CDC and the Child Bureau and sometimes they don't work together. From my perspective, when we got the CDC working with child welfare groups on HIV, it really magnified what we could do. I would hope that people like yourself and Dr. Miller work together because there are so many resources that you could bring to bear.

Ms. Nolan: I want to make sure that you know that we do have a pretty good relationship with CDC through our Federal interagency work group over the years, particularly with our prevention work. In more recent years, they have had more interest in child abuse prevention and focusing on the protective factors.

Dr. Papernik: What would you say to the families that were here today and had so much difficulty with getting support for these kids in the school system? Would you term it a type of abuse at the state or administrative level? Would one of their recourses be to contact your bureau to see if you could intervene on their behalf?

Ms. Nolan: We do get letters from families who feel that their child has a disability and was not well served. We aren't set up to address those educational issues. We would refer it back to our contact person in the state to see if that person could help them and SLOs do help a lot of the time. I totally appreciate the educational issue from my own experience having to go through my sister advocating for my niece to get what she needed. The bureau does not handle educational accommodations.

Dr. Jason: Is it possible for CFSAC members to influence your funding process this year or in the future in order to create a demonstration project on one of the seven or eight things that the committee has been talking about?

Ms. Nolan: We are literally in the thick of doing the grant review for this year. We will be finished with that process by the end of July. We will then immediately start deliberations on what ideas we want to move forward. The decisions on what we're going to consider are made by:

- Looking at all of the different pieces of legislation that we manage. They contain requirements and/or suggestions.
- Evaluating the lessons learned from the discretionary grants that we've already funded. What are we learning from the research? An example: If we gave more money to a regional entity, could it be more responsive at the regional level rather than us managing that response from here? The projects examining that question were very successful and resulted in the creation of several National Quality Improvement Centers that also function as information resources.
- Examining what we've learned from outside groups such as CFSAC.
- Considering the Administration's agenda.

At my level, we present the information. The decisions are made at higher levels.

Dr. Snell: Could you address the specifics of fabricated illness syndrome and how a child will get a diagnosis of that? What would be the process that the parent went through before someone is knocking on their door?

Ms. Nolan: In the past, when the syndrome was called Munchausen, those allegations came to attention of CPS in a variety of ways including physicians and schools officials.

Dr. Snell: I'm wondering about the investigative process. My understanding is that when somebody reports child abuse, they don't necessarily give it a definition.

Ms. Nolan: That's exactly right. Of those 750,000 cases that were substantiated, those were just referrals that came in to CPS or actual reports of allegations. For 2007, 60 percent were neglect, 17 percent were physical abuse, 11 percent were sexual abuse, and 6 percent were psychological abuse. Most systems have some response system protocol set up for how they respond to those reports. In many of the cases there is some kind of medical evaluation, depending on what the concerns are that are being presented.

Dr. Snell: Would they be designated medical professionals who are doing that?

Ms. Nolan: In many locations, yes, including child advocacy centers and children's hospital-based clinics. The American Academy of Pediatricians just created a subspecialty in child abuse and neglect last year. That lends another level of sophistication to the American pediatric community.

Dr. Snell: So they're the group that should be targeted with this information?

Ms. Nolan: I would think so. There are a lot of venues. You can go about it several ways and we've already talked about some of those ways. If you're trying to reach the pediatric community, whether their specialty is child abuse or not, that's the organization to go with.

Dr. Snell: If abuse is reported, are you obligated to investigate?

Ms. Nolan: You're obligated to respond in some way. A greater percentage of the calls that come in are screened out. There's a threshold. In most places there's an intake hotline set up. An interview would take place there to determine whether or not the information gathered suggests that the allegation meets the threshold of the state needing to get involved.

There are many states that are starting to experiment with alternative or differential response. It's called Different Things in Different Places. They offer services even though they did not screen in a case, or they might screen in a case but instead of going the traditional investigative route, they may conduct a clinical family assessment. As I listened to the families today, I wondered what would have happened if the alternative approach response had been used in those cases as opposed to what sounds like a more adversarial response.

Shelley Jackson, Supervisory Attorney. *Department of Education Office for Civil Rights*

Accompanying Documents: *Requirements Under Section 504 of the Rehabilitation Act of 1973; Questions and Answers on OCR's Complaint Process; Protecting Students With Disabilities*

My job at the Office of Civil Rights (OCR) is to work on disability policy issues.

About OCR

- Headquartered in Washington, DC.
- Has 12 field offices throughout United States. Each office has jurisdiction over particular states by geographic area.
- Enforces compliance with two Federal statutes specific to disability:
 - Section 504 of the Rehabilitation Act of 1973 – prohibits discrimination on the basis of disability by recipients of Federal financial assistance.
 - Title II of the Americans with Disabilities Act of 1990 – prohibits discrimination on the basis of disability by state and local governments.
- Entities over which the office has jurisdiction include educational agencies, local school districts, and post secondary institutions.
- We receive approximately 6000 complaints every year involving students at all educational levels.
- More than 50 percent of the complaints that we receive every year involve allegations of discrimination based on disability. Our complaint data don't indicate whether we have had complaints filed on behalf of students with CFS.
- The office does not enforce the Individuals with Disabilities Education Act (IDEA). It is enforced by our sister agency, the Office of Special Education Programs. We coordinate with our colleagues at our sister agency when necessary.

Basic Legislative Principles and Requirements

Who is covered?

Section 504 and Title II protect from discrimination qualified individuals with disabilities. The statutes define disability in one of three ways:

1. Individuals who have physical or mental impairment that substantially limits a major life activity.
2. Individuals who have a record of a substantially limiting impairment.
3. Individuals who are regarded as having a substantially limiting impairment even if in fact they do not.

The interpretation of the term “disability” has been affected recently by the enactment of the Americans with Disabilities Amendments Act of 2008, which became effective on Jan. 1, 2009. A primary impact is that it required that the term “disability” be construed broadly. Congress passed this law because it believed that the Supreme Court and other Federal courts had interpreted disability too narrowly.

Legal Terms

- Neither Section 504 nor the ADA has a statutory definition of “substantially limits.” In the ADA amendments act, Congress said that it wanted the definition of “substantially limits” to be interpreted consistent with the findings and purposes of that statute. If we turn to those sections of the statute, they make clear that

Congress intended to overturn Federal court decisions that it thought had taken too restrictive a view of the term.

- “Major life activities.” Both Section 504 and ADA have non-exhaustive lists of major life activities in their regulations. The fact that an activity was not listed doesn’t mean that it isn’t a major life activity. For example, both sets of regulations include such activities as learning, performing manual tasks, speaking, breathing, and walking. The amendments act added activities to the non-exhaustive list including concentrating, thinking, communicating, standing, sleeping, and reading. The law also added a non-exhaustive list of “major bodily functions” that includes the immune system, the neurological system, and brain or circulatory functions.
- “Episodic impairments.” The amendments act made clear that an impairment that is episodic or in remission is still a disability as long as when active, the impairment would substantially limit a major life activity.
- A disability under these statutes is not the same as having an impairment or a diagnosis. An impairment by itself is not a disability. To be a disability, the impairment must substantially limit one or more major life activities.
- “Qualified individuals with disabilities.” At the elementary and secondary level that really only means that the young person is of compulsory school age.
- “Individuals who are regarded as having a substantially limiting impairment even if in fact they do not.” The amendments act made clear that individuals who are covered only because they are regarded as disabled are not entitled to reasonable accommodations or reasonable modifications.

Obligations That Statutes Impose on School Districts

Under Section 504:

- An elementary or secondary student with a disability who attends a public school is entitled to what the law calls a “free and appropriate public education (FAPE).”
- The regulations say that an appropriate education under Section 504 is the provision of regular or special education and related aids and services that are designed to meet the student’s individual needs as adequately as the need of non-disabled students.
- A student can be protected even if he or she doesn’t need special education so long as he or she needs related services or regular education provided in such a way as to meet that student’s needs as adequately as the needs of other students are met. Example: A student with diabetes who doesn’t need any kind

of specialized instruction but may need the school's assistance in maintaining a medication regimen.

- **Determination of disability** under Section 504 and the provision of a free and appropriate public education is made on the basis of an individual disability. You could apply some of the general legal requirements to what's happening with an individual student with CFS. Are they substantially limited? What are the major life activities that are being substantially limited? How can they be covered? It's not necessary to meet special education to qualify under 504.
- School districts must have in place a procedure for the evaluation and placement of students who may have disabilities. The legal obligation is that school districts must evaluate any child who because of disability needs or is believed to need special education or related services. Evaluations have to be conducted before an initial placement in a regular or special ed program and before any significant change in placement.
- School districts are required to establish standards and procedures that govern the use of tests and evaluation materials including that they are validated for the purpose for which they are used, that they are administered by trained personnel, that they include materials tailored to assess specific areas of educational needs, and that they accurately reflect the student's aptitude or achievement, and not simply their impairment, except where those are the skills that are intended to be measured.

Determination of Type of Services

In interpreting the evaluation data and making placement decisions, school districts must:

- Draw upon information from a variety of sources.
- Establish procedures to make sure that the information is documented and carefully considered.
- Ensure that placement decisions are made by a knowledgeable group of persons who are knowledgeable about the child, the meaning of the evaluation data, and the placement options.
- Ensure that placement decisions are consistent with the legal obligation to provide for the education of students with disabilities with non-disabled students to the maximum extent appropriate.
- School districts may not rely on assumptions regarding persons with disabilities or classes of such persons. The obligation to evaluate, identify, and provide services to students has to be based on their individual needs and schools must place students with disabilities with non-disabled students to the maximum extent appropriate in non-academic and extracurricular activities.

- Establish a system of procedural safeguards that includes notice, the opportunity to examine records, an impartial hearing with a review procedure, all with respect to the identification, evaluation, or placement of students with disabilities.

Any person who believes that a student with CFS or any other disability has been discriminated against on the basis of disability can file a complaint with the appropriate enforcement office of the Department of Education's Office for Civil Rights.

More information is available on our website.

Committee Discussion

Ms. Jackson: Section 504 governs compliance by recipients of Federal financial assistance. The Department of Education gives money to states; often that money is passed to local school districts. We may have other programs where the department gives money directly to local school districts. Receipt of that money carries with it the obligation to comply with Federal civil rights statutes including Section 504.

Title 2 of the ADA is a little different, but the legal obligations still apply. Title II applies to state and local government entities, so there's no requirement under Title II that compliance be linked to the receipt of Federal financial assistance, although as you can imagine, most states and local school districts do somehow get it. That nondiscrimination law also applies as long as the entity we're talking about is an entity of state or local government.

Dr. Snell: Could you expand on the difference between special education and accommodations?

Ms. Jackson: In the real world, it's often six of one and half a dozen of the other. Strictly speaking, special education may be what kinds of educational services you're getting in the classroom, by and large.

Dr. Snell: Is a student going to the library to be taught by a tutor considered special education or an accommodation?

Ms. Jackson: It probably depends how those services are classified by the local school district. I think the bottom line from a legal perspective is what kinds of regular or special education or related aids and services does the student require? The Section 504 Plan is a document that school systems often create to memorialize the nature of the student's disability and what the school is going to do about it.

If it was determined that to provide the student with an appropriate education he or she needed one-on-one tutoring or a modification in his or her schedule, these things would be, if agreed upon, documented in the 504 plan, and from my perception it doesn't really matter whether you call it special education or related services or an accommodation. The idea is that these services and this way of educating the child have been

determined as necessary in order to make sure that the student gets a free and appropriate public education.

Dr. Snell: Where I see a potential issue is the one student whom the school wanted to put in special needs classes. The parents didn't want the student in the special needs classes; they wanted what I would have called an accommodation. They wanted some individual assistance in the regular class. Would that be potentially a civil rights issue?

Ms. Jackson: The shorter answer to your question is that's why Section 504 provides for a system of procedural safeguards, so there is a mechanism for a parent to challenge an evaluation or placement decision. A parent could file a complaint with our office saying that they believe their child was discriminated against on the basis of disability. I will tell you that generally speaking, when we look at the provision of a free, appropriate public education, we are going to look at what procedures were in place, were those procedures followed, was the child evaluated, was there a placement decision, and was there a knowledgeable group of people?

By and large, unless it's an exceptional circumstance, we are not going to get into whether a child should have had five hours of physical therapy this week as opposed to two, because the law is concerned with whether the parents have a mechanism through the system of procedural safeguards for challenging that.

Mr. Newfield: That sounds like you're essentially looking at the procedural aspects of their process rather than evaluating the outcome of that process.

Ms. Jackson: I think that's largely true. I'll point you to the Frequently Asked Questions document that says except in extraordinary circumstances, we do not review the results of individual placement or other educational decisions as long as the school district complies with the procedural requirements of Section 504 relating to identification and location of kids with disabilities, the evaluation of such students, and due process.

Mr. Newfield: What's their recourse if they're not happy with that outcome and do they have to go through you precedent before initiating some other procedure?

Ms. Jackson: No they do not. There's no requirement to exhaust administrative remedies through OCR before pursuing either the procedural safeguards option that the law requires the school district to have or initiating legal action.

Mr. Newfield: So if somebody was dissatisfied with the plan that the school sought to implement and they wanted accommodations rather than an assignment to special education, is that just a legal proceeding where they're alleging discrimination, or are they challenging the outcome?

Ms. Jackson: I think what the parent would likely be challenging is the identification, the evaluation, or the placement decision that was made. I really depends on what the

parent's concern is at which point in the process. The parent goes through due process and says, "I object to this proposed placement of my child in this education setting." Due process is the procedure that the law requires the school district to have. The due process hearing is presided over by impartial hearing officers, so the idea is that there's a neutral third person so it's not just the parent and the school district at loggerheads.

I will get back to you because I know that we've issued guidance about who is and is not an impartial hearing officer. I believe what we've said is that in Section 504, the hearing officer can't be an employee of the school system, but I would be happy to double check that.

Mr. Newfield: What's the recourse to the family when that gets rubber-stamped?

Ms. Jackson: The regulations also say that the hearing process has to have a review procedure. If, for example, the school district is the first level of the due process hearing, there has to be a second level available. If that doesn't work, the parent could consider a legal option. They could file a complaint with us and we would examine whether it would be appropriate for us to open a complaint.

Ms. Artman: This is a broken illness. I think I'm going to adopt Nancy's phrase and name it "broken illness syndrome". This illness saps not just the child's energy; all of the parents' time is spent seeking medical care for an illness that we have no doctors for. It becomes complex two-fold for both of you.

First, the accusation of abuse is also more likely to be true because you have frustrated parents. I'm not accusing any parent in the CFS community of abuse. But because you have a child who is ill, you're more likely to be in an abusive situation from what I understand from what I've read.

The other thing is, because a parent is spending so much of their time either caring for a child or taking him to medical care, when it comes to education, they do not have the energy or time to fight another battle. We want you here because we want to figure out how to fix this. We want to make it simple for every parent who's trying to deal with a medical nightmare that has a perception issue that these are malingering children who are "just whiny", "aren't really sick", and "look healthy to me when they show up in class."

How do we move this very important dialog forward with you to get this done? If we go state-by-state-by-state, that's 50 times we have to have this discussion, and failure or success keeps being repeated. If we can do something at this national level, it makes such a huge impact on so many children's and parent's lives. How do we find a nice fix that we can move forward on and keep working on, and not just discuss it and go back to our lives? Is there anything that we can do interact with you further to keep this moving to find a solution?

Ms. Jackson: I am cognizant as a lawyer that when you sit here and say, “This is what the law requires,” it doesn’t always work out that way. Parents of these kids are struggling with an awful lot. I will go and discuss this with the political leadership of my office—I’m sure they’ll be interested in this experience and what’s going on at HHS—and see whether there would be any interest in some future dialog. I’m not authorized to commit the department to do that as I sit here. We have offices throughout the nation that are involved in complaint investigation but we also try to do a fair amount of outreach, technical assistance, and education. Sometimes it’s better if you can proactively inform individuals with disabilities about their rights and school districts and other recipients about their legal obligations. We have done that.

Dr. Willis-Fillinger: Is there a regular process for training those in the system who are involved in mediation when there are claims of discrimination and challenges with a mismatch of what the parents would want for their child versus what the school thinks would be appropriate? Is there a process for informing those individuals of the latest science, and information about children, and things that they could consider like CFS and how it presents?

Ms. Jackson: I don’t think there’s anything as systematic as you are describing it. Our office at the headquarters level and our enforcement office frequently get requests to come and do technical assistance presentations, although they would be to tell you about the law and legal requirements, not the science.

Ms. Healy: You both mentioned some descriptive statistics in terms of number of persons who go through your systems. Can you provide more specific information related to persons affected by CFS—how many people are coming into the system, how many are successful, and how many are not?

Ms. Nolan: The numbers are pretty gross in our system. I don’t know how specific they get. Certainly we’d be happy to break it down in more detail.

Ms. Jackson: Our complaint database captures some disabilities but not all, and it does not capture complaints about CFS in particular. I will send Dr. Jones a link to our most recent report to Congress, which contains more information about the data of complaints that we process.

(<http://www.ed.gov/about/offices/list/ocr/congress.html>.)

Dr. Klimas: Ms. Jackson, is there any listserv you might have to begin a dialog with the people who would be adjudicating these decisions or the people at the school or school district level? For instance, in the case of the person in each school who is responsible for teaching the IEP process folks what might be considered a valid illness—if just that came across: this is a valid illness—if we could just get that one piece as a rational goal, that would be a very, very helpful thing. Is there an information conduit to the first-line people?

Ms. Jackson: We don't have a listserv in the same way that ACF does. When we issue policy guidance, our way of communicating that, generally, is a post on our website.

Dr. Klimas: Might we have access to a way to post an educational piece?

Ms. Jackson: I will raise that back at my office. It's generally things that we create.

Dr. Klimas: We would offer to work with your office to create such a thing. It's nothing that either of you can fix, but it's a weird system that we have that forces a parent and a child to be their own advocates. When you have a professional advocate to go into the IEP situation and help craft an IEP that's appropriate for the child, that's when it's been successful.

[Dr. Oleske called a break for lunch.]

Dr. Cheryl Kitt, Deputy Director, *Center for Scientific Review, NIH*

Peer Review Update

We're in the implementation phase now of what we have done based on about two years worth of discussion with the public:

All new applications as of the January 2009 submission. If you're unsuccessful the first time, you only get one more chance.

New definition of an early stage investigator.

- The original NIH definition did not take into consideration where an individual was in his or her career stage. The new definition means someone who's junior in his or her career (less than 10 years). That will be tracked because it's important for R01s.
- There are separate pay lines for those individuals. The pay lines are almost twice as good.
- New investigators will be reviewed separately in study sections so that they're not competing against established investigators.

Scoring process is changing dramatically.

For the May review of applications that came in January-March:

- Scoring is now from 1-9 as opposed to 1-5, which will translate into priority scores of 10-90 as opposed to 100-500. The best score that you'll get on your

summary statement is a 10 and the worst score is a 90. That's if the grant proposal was discussed.

- There is no more unscoring. All applications will receive scores. The discussed applications will receive an overall impact score, which is your priority score, in addition to five other scores that you receive for the five criteria that the reviewers will be using to judge your application. The not-discussed group will only get the criterion scores, not the overall impact score.
- What do the numbers 1-9 mean? The overall score is related to impact. Will it make a difference? Will anybody take it, use it, or do it for clinical applications?
- There's no requirement that scores fit under a Bell curve. If all the applications are exceptional, reviewers can score them as such.
- The summary statements or critiques are shorter. The overall size of a critique is only going to be about two pages. Each of the five criteria will get a quarter page. The reviewers have been instructed to write their narrative in bullet form highlighting strengths and weaknesses. The numbers and the critiques should go hand in hand.

We were kind of overcome by ARRA. We consider it a challenge. For those of you who have applied for challenge grants under ARRA, we have received in excess of 20,000 applications. We will be reviewing them in two stages—the technical merit review and the overall review by the panel of experts in face-to-face study sections. All of the reviews will be completed by July 22.

All of the above changes were in place for the May reviews. The only things we haven't officially implemented yet are:

- Short applications for R01s, which will go to 12 pages from the current 25 pages.
- The R21 is currently 15 pages and that will go to six pages.
- Amended applications (resubmissions) for R01s currently get three extra pages as an introduction; you will get just one more page.
- For those of you who do clinical studies, there will be an expanded section E that allows you to talk about everything you need to inform the reviewers about that clinical study.

You should look at the NIH guide to notices every day for news on funding opportunity announcements or changes to policy. The original challenge grants called RC1 and the Grand Opportunity challenges all have to be funded in this fiscal year, so all the reviews will be completed by the end of July to be funded by September 30, 2009.

There are several other requests for applications probably in the works now for 2010. Those have to be issued, reviewed, and funded within 2010. The ARRA stimulus is only for two years. There is extraordinary tracking that's required of successful applicants. There were applicants for ARRA funding in the CFS arena.

Committee Discussion

Dr. Glaser: You mentioned that CFS applications are coming in, which is good news. Have there been changes in broadening the base of people on the SEP to people who actually do CFS research?

Dr. Kitt: We always try to do that. It depends who they're in conflict with and whether they have applications in as well. If you serve on CFSAC, you can't review. We have lifted some of the waivers at this point.

One of the issues that we face is that many of the investigators want to be reviewed in other study sections, not just the CFS SEP, because they would rather be reviewed with their peers. We struggle with this all the time. You need to consider whether the SEP is still serving a purpose for the scientific community. We do the best we can to make sure the appropriate applications are in the right place, but it's the investigators who really are making those choices.

We honor requests. We want investigators to submit a cover letter with their application letting us know where they want their applications reviewed and what institute they'd like to be assigned to in the event it is funded. We honor those 95 percent of the time.

Dr. Klimas: The reason why we can't make a recommendation one way or the other on an SEP has been that we've never been able to access a really important piece of information—what is the rate of approval on a 1st, 2nd, and 3rd round application compared to a standing committee's rate? Without knowing that, it would be hard-pressed for an advisory committee to make a recommendation.

Dr. Kitt: I know in general the answer to your question. In general, applications that go to SEPs do better. They're usually smaller, very focused committees.

Dr. Klimas: The major issue that we've had has been the comment from applicants saying their revised application didn't go back to the same reviewers. It is a concern that you submit the first time and get one set of critiques, you address them, and then you get a second set of critiques that basically ask for the first proposal. That suggests it wasn't the same reviewers.

Dr. Kitt: Possibly. We don't guarantee continuity of review because reviewers turn over, even on standing committees. We can't guarantee that it goes back to the same people and even if it did, they ask for additional comments. The reviewers are looking at this application and the decision they have to make is if science is any better, not whether the applicant addressed the concerns. The applicant believes that if they answer all of the questions and concerns they're going to get funded eventually and that's pretty much what had been happening. But in fact, the impact of the significance of the research wasn't addressed appropriately. If the applicant answered all of the questions, is this something that's going to make a difference? That's what the difference is now in review. The reviewers are going to address that issue.

Ms. Artman: Are you going to be Vista compatible for grants.gov? If you ever find out, that would be great. The CDC has asked us to prioritize some things. Etiology and biomarkers are really important and yet when we look at how many grants are funded in these areas that we consider crucial, the answer is not a lot. Is it within our purview to suggest that when reviewers are assessing the impact that they take those two things into consideration?

Dr. Kitt: We are not allowed to talk about funding or program priorities during a peer review. The reviewers are asked to review the scientific merit of what's proposed. That doesn't mean they don't think about it when they're reviewing. We know that they do.

Dr. Glaser: The problem has been that the people who would be knowledgeable in those areas are not appearing as members of that SEP.

Dr. Jason: The research subcommittee is setting up a conference call with Dr. Kitt, so we'll continue this discussion if we don't get to all the issues. Any progress in terms of selecting a permanent scientific review administrator? Is there any way of getting data about CFS grant proposals that have come in and been funded?

Dr. Kitt: Very few have come in over the last two years. The best thing that you can do as a committee is to encourage scientists to get interested in the problem. We don't see many applications that are explicitly focused on CFS.

Dr. Klimas: And yet when there was a special round several years ago, you had 35 applications. The implication was, just as with these challenge grants, if there is money, people will come. And that's the bottom line. Right now investigators don't perceive there's money and the application process is somewhat futile even though they've been successfully funded in the past. PIs perceive it as of dwindling interest.

Dr. Kitt: I really don't have a magic bullet except to get people interested and excited in finding what's behind the mystery here. Think about a conference bringing in people who don't think about your condition and getting them interested in it. Find one or two investigators and that's one or two more than you had before.

Public Comments

Judy Machacek, New Jersey

Thank you to all members of the committee for allowing me to comment today by telephone. The challenge of travel and a full day of meetings would certainly have been a deterrent to my participation.

I am 55 years old and have had ME/CFS for 20 years after a very serious reaction to Lyme disease. Prior to my illness I worked on Wall Street in a very demanding position as a portfolio manager, trader, and consultant. My job required that I travel to many

cities around the country and around the world. I loved my career and my professional life.

Twenty years ago I was on a plane twice a week and today, unfortunately, I could not drive to Washington, DC, without help. I appreciate that members of this committee truly understand the overwhelming fatigue; pain; headaches; sleep problems; hypersensitivity to light, sound, and medications; and also many other things that define CFS. I am very fortunate because only the first five years of my illness confined me to bed and changed my life so dramatically. Today I can function hours at a time and sometimes feel pretty good for days at a time. But I can never predict or control my good or bad days. I have learned to adapt my daily schedule to my symptoms but please understand that I do not yield to my symptoms, I simply make adjustments. I have a pretty busy and wonderful life.

As a co-leader of a support group in Northern New Jersey, I speak for many when I say that a major issue we have as patients is that our symptoms are not visible to others and even family and friends do not understand why we are “still sick.” The sad truth is that most people have only a short-term compassion for illness, especially when there is so much misunderstanding and a lack of respect for the seriousness of this disease.

Another burden of ME/CFS is the powerful strain on a marriage. This disease and its stigma have destroyed many relationships and marriages. It was not until I became sick that I truly understood my husband’s ten-year struggle with the same illness. Physicians also get frustrated with us because CFS is a complex illness which means time-consuming, which translates into money, and yet there is still no medical test to validate our diagnosis and there’s no treatment that can cure our symptoms. Some doctors don’t want even to be associated with us because of the stigma or because they simply don’t know what to do with us. This is a chronic and unpopular illness that gets very little respect from society or from the medical community and with which both patients and doctors are embarrassed to be associated.

It’s not enough that we just raise awareness of ME/CFS as a medical condition. We really need to change the image and the perception of this illness across all levels of society. We need to reject the notion that this is a mental health condition and articulate the physical symptoms. If you compare ME/CFS to other chronic health conditions like diabetes or MS or even rheumatoid arthritis, there’s no reason why we should be dismissed as a lesser illness. Diseases like FM, Lyme disease, lupus—all of these overlap symptoms with CFS and yet they are not ridiculed by society. Why is that? We don’t know. Perceptions must change so that patients and doctors can stop wasting time proving that people are sick and focus on improving their lives.

People come to our support group desperate for acknowledgement and validation of their illness. They need information on treatment and cure. They need doctors who are compassionate and knowledgeable about ME/CFS. Unfortunately we cannot always give them the answers they need. Please help us to change this situation. I would like the committee to consider these requests:

1. We need to verify and validate our condition, hopefully with a blood test but possibly with a test for the physical imbalances that define our condition.
2. We need to remove the diagnosis of being “tired” and define CFS with appropriate medical terms, perhaps describing it as a dysregulation of the immune, endocrine, or neurological systems.
3. We need to educate senior executives in the medical community about the seriousness of this illness.
4. We need ME as a priority topic in physicians’ programs for continuing medical education to develop their understanding of CFS so they learn to treat us through medication and coping therapies.
5. We need to remove the stigma of this disease and acknowledge CFS as a legitimate illness. Once that happens, the funding, research, treatments, and acceptance will follow.
6. We need to enforce a legitimate diagnosis of CFS among insurance companies so they don’t deny medical treatments or disability.

I thank you very much for allowing me to share my experiences and ideas with you today. We really appreciate all you have accomplished in the past ten years to fund research and bring discussion of ME/CFS to this committee level. Much progress has been made, but we need to do more to help the millions of patients like myself who expend precious and limited money and energy to cope with this debilitating illness.

Claudia Goodell

Good afternoon members of the committee as well as member of the CFS patient population. My name is Claudia Goodell and I have CFS and FM. I also have a bachelor’s degree in psychology with a minor in American Sign Language and a master’s degree in audiology. I am an accomplished artist and a fit athlete. I have always considered myself a pioneer of change and have applied by influence in situations I believed required more forward thinking.

I pushed myself to become the first female grocery stacker at the local Piggly-Wiggly at the age of 16 and the first female in the high school weight lifting class. During graduate school, I initiated the addition of a course in counseling to be added to the curriculum for the audiology program. Following an eight-year career in audiology, I enjoyed three successful years working in the pharmaceutical industry, where I was recognized and rewarded by my peers and management until CFS made this impossible.

I fought the onset of CFS like a lion. In the face of unrelenting fatigue and constant pain, I continued to push myself to go to work until I no longer could. I battled cognitive dysfunction while working as a pharmaceutical representative, not understanding why I was suddenly struggling to recall standard vocabulary. Standing upright became difficult. Although my doctors and I suspected CFS, this diagnosis would not come for months, as I was constantly pressured by my company to return to work or resign. I

was told that a diagnosis of CFS would entitle me to three days off; however, a diagnosis of depression or cancer would allow more.

Exhausted, confused, and without a proper advocate, I was ill-equipped to wage the necessary battle against my employer for the long-term disability benefits that I should have been granted and that I was entitled to receive. Instead, I was forced to resign.

Unrelenting fatigue and disabling pain shattered my ability to be a traditional wage earner and forced me to receive a pittance of a monthly disability check. CFS reduced me from the rewarding position of a professional to the unfamiliar territory of being completely dependent on my husband for income and health insurance. With my limited functional time I am forced to complete necessary mundane tasks while sacrificing the things that bring me joy.

Pacing my energy has become a daily practice. There is a constant question of whether I will get enough sleep, proper nourishment, and sufficient water intake to stave off the secondary issues of a sleep disorder, chronic migraines, irritable bowel syndrome, and chronic infections. In addition to supplements, I rely on a prophylactic prescription medication to treat my migraines and chronic pain. Western medicine offers few or no solutions to this situation, so instead I have been forced to seek treatment through methods such as weekly therapeutic massage, acupuncture, chiropractic treatments, yoga, and meditation.

CFS is a thief of time that reduces a functional day to a fraction of that of a normal health person. It's an energy crisis that forces us to sacrifice the things that bring us joy and are often taken for granted. CFS has relegated four million Americans to be partial participants in life. It has stripped our ability to contribute as well as forced us to be a drain on society. I am learning to accept CFS; however, I still wage war against the total lack of control I have over my own life. I am a keen mind trapped in a dysfunctional body, treading in a society that is mostly unaware of CFS and the scope of its violation.

Without public recognition of CFS, progress towards approved treatment options is hopeless. We must shake the ground enough to gain the necessary attention to solve CFS. We must provide public awareness messages to gain acceptance of CFS as a real illness with a biological basis. We must provide education in order for patients to be diagnosed early and properly. We must educate healthcare providers so that they are comfortable and competent in diagnosing and treating CFS. Proper research must be conducted to find the cause of CFS as well as to develop safe and effective treatments for the disease.

With regard to CFS, previous efforts made by the CDC have been static and my hope is that with the new appointments to the Federal health agencies, the ground beneath CFS will become more dynamic.

So although I am plagued with CFS and ME, I am also a successful educator, an avid cyclist, an accomplished artist, a wife, a mother, a daughter, and a sister. I implore this committee to hold the CDC accountable for their past negligence as well as the future direction of the CFS research program.

Thank you for your time.

Dr. Fred Freidberg, Buffalo, New York

As the president of the IACFS, I would like to thank the CFS Advisory Committee for this opportunity to comment on the CDC's five-year strategic plan for CFS research. The new director at CDC has the opportunity to reinvigorate CFS research as well as reinstate CFS as a public health priority. This was emphasized by Dr. Judy Gerberding at the November 2006 launch of the CDC's public awareness campaign.

Unfortunately the CDC's draft five-year research plan lacks sufficient substance and detail. As such, we are unable to directly respond to or endorse this plan. Rather, we suggest a single critical change in the CDC program. That change is to make CFS a public health priority. The IACFS requests that the CDC declare CFS a public health priority. To achieve this goal, the CFS community needs strong and visionary new leadership from the CDC, the recognized world public health authority, to remove the enduring stigma associated with being a patient. This stigma and skepticism about the illness is also a deterrent to those professionals who would consider entering the field of CFS as researchers or clinicians.

CDC's own epidemiologic studies have identified more than a million CFS sufferers in the United States with as many as 85 percent still undiagnosed. Further, the CDC has indicated that CFS is a debilitating illness with an annual economic impact of at least \$9.1 billion. Yet CDC sponsors no prevention or clinical treatment research. This is a major concern given these three points:

1. The large number of severely ill and undiagnosed patients.
2. The inadequacy of current subjective diagnostic criteria for CFS.
3. The absence of effective, evidence-based treatment options.

We have put together recommendations that the CDC can enact to make CFS a public health priority:

1. The CDC needs to identify a CFS program leader who is a progressive, open-minded, and dynamic manager with a sense of urgency commensurate with the pressing needs of the CFS community.
2. The CDC should undertake high-profile public and professional awareness campaigns to fully legitimize the illness of CFS and reduce its stigma.
3. The CDC should support extramural research into the pathophysiology of CFS in order to achieve the critical goal of objective diagnosis and effective treatment. Such efforts should eventuate in the identification of biomarkers. Biomarkers will

justify a new, objective case definition and the re-labeling of CFS with a more appropriate and credible name.

4. In the spirit of public resource sharing, the CDC should make available its study protocols and the epidemiologic clinical and laboratory data from all studies conducted by the CDC's CFS research program since 1984.
5. The CDC should abandon its use of the empirical case definition for CFS and make a public statement to this regard. The empirical case definition has been highly criticized by expert CFS epidemiologists because it is overly broad and based on subjectively determined criteria.
6. The CDC should take a proactive leadership position by exploring its potential role in developing an international clinical trials network in collaboration with clinicians, private industry and university-based researchers.
7. The CDC should partner with the IACFS—the only national and international professional organization representing investigators and clinicians—to develop evidence-based diagnostic and treatment guidelines for management of CFS.

We thank the CFS Advisory Committee for this opportunity to comment on the CDC's five-year research plan. Both the CDC and IACFS should work together to achieve our mutual goals of establishing new evidence-based research programs, improving clinical care, and offering comprehensive provider healthcare education. Our ultimate objectives are to eliminate the suffering caused by CFS and to work towards the eradication of this serious illness.

Thank you.

Dr. Oleske: What is membership of your group?

Dr. Freidberg: Five hundred biomedical and behavioral professionals.

[Public commenter Brian Smith was absent from the meeting. Dr. Jones closed the public comment period and opened committee discussion.]

Discussion and Development of Recommendations

[CFSAC adjourned for 20 minutes so that subcommittees could caucus on recommendations.]

Dr. Jason presented the Research Subcommittee's recommendation:

- *We have heard from the IACFS/ME President, who represents the scientific CFS community, call for new leadership within the CDC's CFS program. We also learned that a CFS patient group has over 1,000 signatures asking for a change in leadership at the CDC's CFS program. Furthermore, we continue to hear complaints from patients during public testimony about a number of issues involving the leadership at the CDC. In addition, a number of patient*

organizations have called for a change in leadership at the CFS CDC program. We are concerned with the input from these diverse groups. We also felt that the five-year plan offered at our CFSAC meeting was ambiguous concerning what could be accomplished with available resources and also seemed to lack a bold vision to significantly advance the field. We recommend to the Secretary that the Director of the CDC consider these issues before the five-year plan is implemented and consider taking appropriate action.

Dr. Jason noted the ongoing debate over how specific CFSAC recommendations should be and said that his subcommittee was trying to give direction while at the same time avoid dictating what the HHS Secretary should do.

Various members discussed:

- Defining the phrase “take appropriate action.”
- Citing Dr. Reeves by name.
- Specifying the Secretary of HHS as the official who should take action.
- Expressing concern, if a change in CDC leadership takes place, over who will step up, whether or not there is someone willing to step up into that role, and what will happen as a result.
- Use active language at the beginning of the recommendation that states that the five-year plan and CDC leadership are inappropriate.

Dr. Jason said that the recommendation implicitly recognizes that any new leadership should have bold vision. He expressed concern over being too prescriptive about what CFSAC wants the Secretary to do.

Dr. Willis-Fillinger pointed out that the recommendation does not describe what went wrong, exactly what CFSAC would like to see done, and what bold, progressive leadership would look like. She said that the recommendation is subjective without any information on which the Secretary could take aggressive action. She suggested discussing substantive items that members would like to see in the five-year plan and providing examples of progressive leadership.

Mr. Newfield added that CFSAC should include its vision rather than just being critical. **Dr. Jason** commented that the committee did not have enough time to produce detailed recommendations during the current meeting. He said that the subcommittee could draft specific items between meetings, but that would mean a six-month delay in final CFSAC approval. Members discussed approving the broad recommendation while including specifics in the meeting minutes.

Dr. Klimas said that the CDC “came to us hat in hand and said, ‘We want your advice on our five-year plan with specifics.’” She said that to respond with such an ambiguous recommendation “is not good enough” and that the committee should “do a proper job of it” even if that meant crafting specifics over the next six months. She suggested that the committee pay attention to the CDC’s request for research priorities and carefully

consider that the process of changing leadership may adversely affect the research program or its funding, depending on how the change takes place.

Dr. Oleske pointed out that the format followed in the past by CFSAC was to have a recommendation that was one or two sentences long followed by the reasoning behind that recommendation. He suggested that the committee follow such a format with the recommendation under consideration.

Mr. Newfield suggested that the committee may want to table the recommendation so that CFSAC members could flesh out specific research priorities and “put together our vision.” He favored crafting a strong recommendation rather rushing through “a watered-down criticism.”

At **Dr. Klimas’s** suggestion, CFSAC members decided to consider the Education Subcommittee’s recommendations to see if some material could be incorporated into the recommendation already under consideration. **Ms. Healy** presented the subcommittee’s two recommendations:

- *Establish progressive leadership at the CDC that can achieve progressive, meaningful progress in CFS research, clinical care, and education.*
- *Provide adequate funding to CDC to effectively carry out a detailed five-year plan. This should include immediate progress in these areas:*
 1. *Identification of biomarkers and etiology of CFS.*
 2. *Partnership with organizations representing CFS scientific expertise to create guidelines for adult and pediatric management.*
 3. *Provide web-based guidelines for CFS management given our current state of knowledge and expert opinion.*
 4. *Provide comprehensive information about CFS in partnership with CFS experts to the scientific community, medical and mental health providers, educational institutions, and the public for both adult and pediatric CFS through HHS resources.*

After further discussion on language and content, CFSAC unanimously approved the following recommendation. Members agreed that specific numbers of testifiers and organizations could be added during editing:

Recommendation #1

Establish progressive leadership at the CDC that can achieve progressive, meaningful progress in CFS research, clinical care, and education.

We have heard from the IACFS/ME President, who represents the scientific CFS community, call for new leadership within the CDC’s CFS program. We also learned that a CFS patient group has over 1,000 signatures asking for a change in

leadership at the CDC's CFS program. Furthermore, we continue to hear complaints from patients during public testimony about a number of issues involving the leadership at the CDC. In addition, a number of patient organizations have called for a change in leadership at the CFS CDC program. We are concerned with the input from these diverse groups. We also felt that the five-year plan offered at our CFSAC meeting was ambiguous concerning what could be accomplished with available resources and also seemed to lack a bold vision to significantly advance the field. We recommend to the Secretary that the Director of the CDC consider these issues before the five-year plan is implemented and consider taking appropriate action.

Ms. Wiley made the following comments about the Education Subcommittee's recommendation on the CDC's five-year plan:

- The CDC does not provide its own funding, Congress does.
- Although CFSAC members had not received plan copies prior to the meeting, when members have a chance to read it they will discover that some of the Education Subcommittee's concerns will be addressed.
- The plan may not be as specific as CFSAC members would like, but it is a draft document and the CDC is seeking members' specific input on what is already included.

Dr. Bateman said that she referred to the five-year plan when drafting the list of most urgent needs given the available resources. The list is not meant to cover the whole five years, she continued. The four items are immediate progress suggestions.

Dr. Jason suggested that the committee vote on the recommendation then provide a more thorough reaction at a later time. He asked Ms. Wiley if the CDC needed the committee to specify the level(s) of leadership in its recommendation. **Ms. Wiley** responded that CFSAC is getting into a branch-level personnel decision and she was not sure about the appropriate level of detail for a formal recommendation to the Secretary of HHS.

Dr. Jones noted that the while the CFSAC charter permits delving into personnel matters that the committee believes need attention, the HHS Secretary would likely want to focus on outcomes—where the recommendations are meant to lead. The Secretary would then take the action or formulate a directive as she deems appropriate.

Dr. Klimas told **Ms. Wiley** that the recommendation represents the immediate issues that should start to be addressed by the CDC within the next six months. The CDC appropriately requests more thoughtful responses from committee members individually and as a group and subcommittees would be formulating more specific ideas over the next six months, said Dr. Klimas. The recommendation is meant to respond to the CDC review that is underway right now. **Ms. Wiley** noted that the CDC would be happy to participate in any subcommittee discussions. She assured CFSAC members that the five-year plan would not be set in stone over the following six months.

Dr. Cavaille-Coll urged CFSAC to leverage all of the work that has been done by the committee since 1994, including the many recommendations that have been made repeatedly over the years. He said that the CDC has created “one of the best” websites on CFS, including information on guidelines and treatment, but technology has changed and it is probably important to improve on that information. When CFSAC makes a recommendation, it should take into consideration the work that the committee has already done on the subject. **Dr. Oleske** suggested that such information might be included in recommendation preambles. **Dr. Bateman** commented that “there is very little about [CFS] management on that website anywhere” and the subcommittee recommendation is about development and provision of management guidelines.

CFSAC unanimously approved the following recommendation. Members agreed that a preamble will be included discussing past recommendations that cover similar topics:

Recommendation #2

Provide adequate funding to CDC to effectively carry out a detailed five-year plan. This should include, but not be limited to, immediate progress in these areas:

- 1. Identification of biomarkers and etiology of CFS.***
- 2. Create guidelines for adult and pediatric management in partnership with organizations representing CFS scientific and clinical expertise.***
- 3. Provide web-based guidelines for CFS management given our current state of knowledge and expert opinion.***
- 4. Provide comprehensive information about CFS in partnership with CFS experts to the scientific community, medical and mental health providers, educational institutions, and the public for both adult and pediatric CFS through HHS resources.***

Quality of Life Subcommittee

Mr. Newfield: We were looking back at all the recommendations in the spirit of recycling because we’ve beaten the drum for a long time. We were advised by Wanda to think big. The issue of centers of excellence keeps coming back. We talked about it in May 2007 as our first recommendation and at a number of other meetings. In May 2007 we had a long-winded discourse about how important it is. I’d like to have this entire recommendation lifted and readopted. The last paragraph could be changed to say that we understand that there’s stimulus money that might be available that would help both stimulate the economy with jobs and help in the development of science.

Dr. Oleske suggested that the specific number of centers be removed in favor of “regional care centers.” **Dr. Klimas** suggested adding that the centers could “serve as demonstration projects to integrate clinical care, research, and training opportunities.”

Dr. Oleske said that he would craft the recommendation to include Dr. Klimas’s language and circulate the edited recommendation to committee members. He

summarized that CFSAC wants to endorse a concept that it has already recommended four other times.

Recommendation #3

HHS establish 5 regional clinical care, research, and education centers, centers which will provide care to this critically underserved population, educate providers, outreach to the community, and provide effective basic science, translational and clinical research on CFS.

Dr. Klimas requested guidance from *ex officio* members on the need to find another term for “centers of excellence” since the term will no longer have the same meaning at NIH. **Dr. Jones** noted that both “centers of excellence” and “demonstration projects” are loaded terms, the latter implying that they are demonstrating something and when they’re done, they go away. **Dr. Oleske** said that the language would be tweaked later based on what would be the most likely to be funded. **Dr. Jones** assured CFSAC members that the language would reflect that latest and most appropriate terminology and that members would be able to review that language before the recommendation becomes final.

Ms. Artman suggested that subcommittee chairs report back on their members’ more specific feedback for the CDC five-year strategic CFS research plan. **Dr. Oleske** requested that chairs provide him with their feedback to be polished by him and Dr. Jones before submission to the CDC.

Dr. Jones concluded with several housekeeping matters:

- She thanked viewing audience members for their feedback on the first-ever CFSAC web cast.
- She encouraged everyone to bookmark the CFSAC website and watch for updates as more meeting material is uploaded.
- She noted that CFSAC would be calling for nominations during the summer in preparation for rotating some members off the committee in early 2010.
- She noted that the web cast archive link will be posted on the CFSAC website. She added that the website is the “heart and soul” of the committee and “we are doing everything we can to keep it fresh and useful to everyone.

Dr. Oleske thanked members of the CFS patient community for attending the meeting. He added that the next meeting would be his last as chair and reminded members to think of possible nominees.

Adjournment