CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE

Meeting

Wednesday, May 16, 2007
9:00 a.m. to 5:00 p.m.

Thursday, May 17, 2007
9:00 a.m. to 3:45 p.m.

Room 800, Hubert H. Humphrey Building
200 Independence Ave, S.W.
Washington, D.C. 20201

Agenda Wednesday, May 16, 2007

9:00 a.m.	**Call to Order** **Opening Remarks** **Roll Call**	Dr. James Oleske *Chair, CFSAC* Dr. Anand Parekh *Executive Secretary, CFSAC*
9:15 a.m.	**New Member Introduction**	Dr. James Oleske
9:30 a.m.	**CFSAC Community/ Organizational Updates**	
	OFFER	Linda Milne
	Albany Health Management Associates, Inc.	Patricia Fennell
10:30 a.m.	**Update on CFS Treatment**	
	VA Medical Center, Charleston, SC	Dr. Joseph John, Jr.
11:00 a.m.	**Break**	
11:15 a.m.	**Update from NIH**	
	Roadmap Initiative	Dr. Alan Krensky
12:00 Noon	**Lunch**	
1:00 p.m.	**Update from the CDC**	
	CFS & CDC Organizational Structure	Dr. Joanne Cono Dr. William Reeves
2:00 p.m.	**Update from the CDC**	
	CFS Public Awareness Campaign	Dr. Fred Fridinger
3:00 p.m.	**Break**	
3:15 p.m.	**Ex-Officio Updates**	FDA, SSA, HRSA

4:00 p.m.	**Committee Discussion**	
5:00 p.m.	**Adjournment**	

Agenda Thursday, May 17, 2007

9:00 a.m.	**Call to Order** **Opening Remarks** **Roll Call**	Dr. James Oleske *Chair, CFSAC* Dr. Anand Parekh *Executive Secretary, CFSAC*
9:15 a.m.	**Committee Discussion**	
11:00 a.m.	**Subcommittee Reports**	
12:00 noon	**Lunch**	
1:00 p.m.	**Public Comments**	
1:45 p.m.	**Committee Business**	
3:45 p.m.	**Adjournment**	

U.S. Department of Health and Human Services

CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE Meeting

May 16-17, 2007

Room 800, Hubert H. Humphrey Building
200 Independence Avenue, S.W.
Washington, D.C. 20201

Members in Attendance

CFS Advisory Committee Members

Chair

James M. Oleske, MD, MPH, CIP Term: 01/03/06 to 01/03/09

Voting Members

Rebecca Artman	Term: 01/03/06 to 01/03/09
Lucinda Bateman, MD, PC	Term: 01/03/06 to 01/03/09
Ronald Glaser, PhD	Term: 04/01/07 to 04/01/11
Arthur J. Hartz, MD, PhD	Term: 04/01/07 to 04/01/11
Kristine Healy, MPH, PA-C	Term: 01/03/06 to 01/03/09
Leonard Jason, PhD	Term: 04/01/07 to 04/01/11
Nancy Klimas, MD	Term: 04/01/07 to 04/01/11
Jason Newfield. Esq.	Term: 07/01/06 to 07/01/09
Morris Papernik, MD	Term: 01/03/06 to 01/03/09
Christopher Snell, PhD	Term: 04/01/07 to 04/01/11

Ex Officio Members

Centers for Disease Control and Prevention (CDC)

William C. Reeves, MD *(Primary)*
Chief, Viral Exanthems and Herpesvirus Branch
National Center for Infectious Diseases

CDR Drue H. Barrett, PhD (*Alternate)*
Deputy Associate Director for Science
National Center for Environmental Health

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 Officer)*

Anand K. Parekh, MD, MPH
Senior Medical Advisor
Office of Public Health and Science

Invited Speakers

Linda Milne, Organization for Fatigue and Fibromyalgia Education & Research (OFFER)
Patricia Fennel, Albany Health Management Associates, Inc.
Joseph John, Jr., Veterans Administration (VA) Medical Center, Charleston, SC
Alan Krensky, MD, Office of Portfolio Analysis and Strategic Initiatives (OPASI)
Joanne Cono, MD, Centers for Disease Control and Prevention (CDC)
Fred Fridinger, DrPH, CHES, CDC

Wednesday, May 16, 2007

Call to Order/Opening Remarks/Roll Call

Dr. Anand Parekh

Dr. Parekh called the Chronic Fatigue Syndrome Advisory Committee (CFSAC) meeting to order and conducted a roll call of voting and *ex officio* members to establish a quorum. All members were present except Dr. Arthur Hartz, who was in transit.

In his opening remarks, Dr. Parekh noted that CFSAC was chartered in 2002 to advise and make science-based recommendations to the Department of Health and Human Services (HHS) Assistant Secretary, currently John O. Agwunobi, MD, and Secretary, currently Michael O. Leavitt.

Dr. Parekh welcomed new CFSAC members, greeted those who were returning as voting and *ex officio* members, and thanked Dr. James Oleske for agreeing to chair the committee. Dr. Parekh also acknowledged members of the public in attendance, outlined the two-day agenda, and discussed items provided in the meeting folders distributed to CFSAC members. These items included:

- The CFSAC Charter.
- Minutes from the November 2006 CFSAC meeting.
- Speaker presentation materials (listed below preceding each individual's testimony).
- "Putting Chronic Fatigue Syndrome's Myths to Bed," an article from the *ACP Observer* (Vol. 27, No. 4, pp 20-21, May 2007) featuring Drs. Lucinda Bateman and Nancy Klimas and former CFSAC member Dr. Anthony Komaroff, among others.
- Three statements from members of the public who could not attend the meeting:

    - *Statement to the CFS Advisory Committee* from Catherine Morgan, CFS Advocate.
    - *Letter to Dr. Parekh and the CFSAC*, from Cecelia Blair, member of the Vermont Chronic Fatigue and Immune Dysfunction Syndrome (CFIDS) Association of America.
    - *Thoughts on CFIDS in Vermont* from Rik Carlson, CFS helpline volunteer operator.

In response to a committee member's request, Dr. Parekh agreed to provide electronic copies of presentations, statements, and other meeting documents whenever possible.

Dr. James Oleske

Dr. Oleske recognized and thanked the five new CFSAC members [Dr. Hartz was in transit at the time of the introductions]:

- Dr. Ronald Glaser from Ohio State University, who adds an expertise in neuropsychoimmunology as it relates to CFS.

- Dr. Leonard Jason, Director of Community Outreach for DePaul University, which has been researching CFS as it relates to adolescents and quality of life.

- Dr. Nancy Klimas, an immunology expert who has been a CFS leader in the national and international science community for more than a decade.

- Dr. Christopher Snell, professor at University of the Pacific, who has focused extensively on quality of life issues.

Noting Dr. Snell's expertise in quality of life, Dr. Oleske asked all new members to consider on which of three CFSAC subcommittees they would like to serve—Research, Quality of Life, or Education. Dr. Oleske predicted that when subcommittee reports are given on meeting day two, members would recognize that while much has been accomplished, "we have an awful lot still to do." He said that the subcommittees can be productive in guiding CFSAC toward recommendations.

CFSAC Community/Organizational Updates

Linda Milne, *Organization for Fatigue and Fibromyalgia Education & Research (OFFER)*

The motto of OFFER, which is headquartered in Salt Lake City, UT, reflects its purpose: Offer hope. Milne had been living with CFS for five years when she moved to Utah in 2001 and got referred to Dr. Bateman at the Fatigue Consultation Clinic in 2002. Her referral coincided with Dr. Bateman's launching of OFFER. The organization's successes include:

- **Attracting a high-quality board of directors.** The board's executive committee includes Dr. Bateman, the executive director; Stuart Drescher, PhD, board chair, who has struggled with CFS and become a premier clinical psychologist serving the CFS community; and Ted Kaly, whose adult son John developed CFS midway through his doctoral work in art history at Duke University. Other board members include Milne as well as a physician specializing in fibromyalgia (FM); school district executives; a retired educator; an executive with the largest bank in Utah; an attorney specializing in disability issues; and two husband/wife teams, both of whose daughters are ill.

- **Demonstrating that people with CFS benefit** by having connections to both physicians and to mental health professionals who can help them retool their thinking to encompass the realities and possibilities of life that come with CFS.

- **Holding monthly educational meetings** (approximately 60 to date) recorded by an audio-visual team so that presentations can reach an audience beyond the 150+ who attend in person. These include CFS and FM patients, their families, and friends. Presentations are from experts who present therapeutic and coping strategies as well as panels of patients and their caregivers. Dr. Bateman is featured twice a year. Meetings also function as networking opportunities for mentoring and exchanging contact information. Group members arrange for people to have rides to doctor appointments and meetings.

- **Compiling a database of several thousand people** that allows distribution of a monthly e-newsletter complete with links that include the latest information on CFS and FM. The newsletter is a vital tool in the organization's effort to offer hope, particularly to those who cannot come to educational meetings and conferences.

- **Presentation of four annual conferences** focusing on advances in treatment and understanding of CFS and FM through presentations delivered by renowned clinicians, researchers, and scientists in the physical and mental health arenas. OFFER conducts two separate conferences at the same time—one for care providers and the other for patients and their families/friends. Dr. Bateman, her staff, and board members managed the full workload of the provider conference. Milne mentioned the educational benefit of the *ACP Observer* article in furthering OFFER's goal of provider education, especially to internists and family practice doctors. Dr. Reeves visited the University of Utah two weeks ago at the request of Dr. Bateman, completing grand rounds and speaking to 150 physicians. Volunteers, most of whom have CFS or FM, organized the patient conference under Dr. Bateman's leadership.

- **Distribution with the help of the CFIDS Association of conference information** to the public from through broadcast and print media including the top stations and newspapers in Salt Lake City. OFFER distributed public service announcement (PSAs) and press releases throughout the state. The organization heard back from several small counties. People often travel several hundred miles to attend the conferences.

- **Attendance of Sen. Orrin Hatch (R-UT) at this year's provider conference** at Dr. Bateman's request. Sen. Hatch closed the provider conference and opened the patient conference. OFFER's board presented him with a plaque expressing gratitude for his leadership and advocacy for CFS.

OFFER's warm relationships with all CFS Associations, the Fatigue Consultation Clinic, and the University of Utah allow its members to have access to the latest information throughout the nation and the world, said Milne. The clinic, for example, will conduct FM drug studies for several pharmaceutical companies while continuing to be one of only three sites offering ampligen treatment for CFS patients. The University of Utah is also conducting groundbreaking research, and several OFFER board members have passed along information to these scientists through education meetings, e-newsletters, and conferences.

Milne used a personal story to illustrate the effect of OFFER outreach. She was referred to Dr. Bateman by a physician whose daughter had FM. The physician admitted to Milne that he did not believe that CFS and FM were physical illnesses. He said that he tried to raise his daughter's spirits and encourage her to try harder, be grateful for what she has, and push on with her life. He encouraged Milne to do the same.

That doctor attended OFFER's first conference in spring 2002. He left a changed father and doctor, said Milne, after hearing clinicians and researchers talk about the physical devastation that comes with CFS and FM. He asked for and received his daughter's forgiveness and shared his findings with her husband, who was also a "disbelieving MD."

Milne handed a brochure for the 2007 OFFER conference to a neighbor, who began crying on the spot, admitting that despite her family doing the best it can, "mostly I suffer alone. I feel so

isolated." The woman attended the conference and left "with a very big smile on her face…and lots of educational materials in her hands."

Milne told the committee that OFFER's model is effective and its successes with advocacy, patient education, and research should be shared with the other regions in Utah and other states. She concluded that with adequate financial resources, OFFER's model could be duplicated, offering hope to patients, helping families understand the illness, and informing providers about diagnostic and treatment possibilities for CFS.

Committee Members Q&A

Dr. Oleske commended OFFER's work, then asked for the breakdown of the group's 2000-person database by age, noting that school systems are often unreceptive to a diagnosis of CFS in adolescents, and elderly patients are seldom discussed.

Ms. Milne: There are no breakdowns available. At nearly 65, I am one of the oldest people in the database. We have a pediatric problem with CFS in Utah. One of Dr. Bateman's PAs and a psychologist in the Salt Lake area meet from time to time with teenagers and college students with CFS and FM. Just from eyeballing conference attendees, I conclude that I'm on the high end of the age scale, but there are many teenagers and college students who are burdened with this illness. When I look out into the audiences attending education meetings, I see a lot of people probably in their 40s and 50s. My personal concern about research moving forward for CFS is not so much for myself, but for the young people who I keep meeting who are desperately trying to get through high school and get their college education. I meet people who are beginning families who are suffering with CFS while raising young children.

Dr. Jason: The National Institute on Aging (NIA) is sponsoring a conference on fatigue that will include Dr. Gudrun Lange. That might be a contact person at NIA who might have a lot of interest in CFS.

Dr. Hanna: I will also be attending.

Dr. Jason: I am intrigued and excited by your comment that the OFFER model could be replicated in other places. Have you made any efforts to secure the funding to do so? If not, what are the barriers? From what you're saying, if we had 20 sites like this around the country, it would make a big difference.

Ms. Milne: I am hoping that that becomes the next focus of our board. I know that I share this view with at least some of the other board members. I got a feel for it when I was sending PSAs and press releases around the state. I talked to editors of small papers that represented communities that are not heavily populated and heard that there is interest and need. Through our efforts, I think that we really have encapsulated the most important activities in reaching our constituency. I do feel personally that it is packagable. We have not asked for money to do so; I don't know where we would ask, but I know we will find out. If any of you have ideas, I would like to take them back to my board.

Dr. Klimas: I had the pleasure of attending several of the OFFER events, including the most recent one. The thing that I came away with was the intense interest of the providers. What *they* want to come away with is walking orders on how to treat this illness appropriately. This is an extraordinary conference and the providers were given exactly what they need to go back

and start taking care of patients. Even if they've never taken care of patients before, I think that they could have walked away from that conference knowing how to approach the illness. That was a very packagable agenda. I think it absolutely has to be done. The CDC/CFIDS outreach is a wonderful program in a one-hour format during grand rounds, but it is like the "open door." A full day or a day and a half conference for providers that can be offered regionally, would be well attended.

Ms. Milne: That is the importance of having a standard bearer like Cindy Bateman. OFFER would not be the kind of organization that it is without her point of view that when we talk to patients and providers, we must give them how's and what-furs. Providers must leave conferences with know-how.

Dr. Papernik: Why are the providers in Utah more interested in going to these conferences as opposed to those in other states? Are they getting [Continuing Medical Education (CME) credits] for this?

Dr. Bateman: They are. We make this a multi-disciplinary conference, and offer at least six kinds of continuing education for nurses, social workers, psychologists, physicians, and family practice doctors. We've done it through a different CME provider every year on purpose to involve more institutions in this effort. We've used a major health care company and we used the Utah Medical Association last year. This year we did it through the VA, which is involved with the university. Because of this, the university wants to host the conference the next time, which is a huge advance.

It isn't easy to attract providers. The key factors for success are:

- Making the conference multi-disciplinary.
- Advertising. We printed 10,000 brochures and mailed them to 6000 physicians, targeted to the people we wanted to come. We had 150 people attend the conference, which is a good number.
- A great agenda. Thanks to the IACFS/ME and everyone who offered to speak, the quality of the program was excellent.
- A lot of hard work. The fact that the clinic and OFFER are there also raises awareness and helps attract people, but it's still a challenge.

Dr. Papernik: It sounds like Dr. Bateman sees every CFS patient in the state of Utah. If most of these people in the group (OFFER) are her patients, then she probably has the database that Jim (Oleske) was looking for.

Dr. Bateman: My patient database and the one for the conference are completely separate. I *am* able to use my mailing list to send things myself to my patients to advertise the conference, and so are the other professionals on our board, which is helpful.

Dr. Snell: One other thing that an organization like OFFER can do for potential research is provide a database of patients. We can only do research if we can provide subjects, and sometimes that can be difficult. It can be helpful to educate providers to refer patients for research purposes and also for patients to volunteer. They get to understand how important the research can be and how important their cooperation is. We've even traveled to Utah to access Cindy's patient database because we sometimes struggle to find enough patients to populate a study.

Dr. Bateman: At the conference we've had patients volunteer to be on a research list. When we hear about it, we'll list it, allow patients access to the information, and then they can pursue it on their own. It has become a great resource for the university, for example.

Mr. Newfield: Given that the VA was involved in the OFFER conference, does that help in any way in packaging this regionally? It may make it reproducible if you're linking with another agency.

Dr. Bateman: The VA has great resources because they could email everyone. The costs were entirely different. The VA provides the CME free to all CME employees. We were able as a nonprofit to do better financially on the conference. Sometimes commercial CME departments keep all of the money after doing a conference. We had a great partnership with the VA and they increased our resources tremendously, especially in the ability to attract people to the conference and their affiliation with the university.

Ms. Healy: I was curious about what work OFFER might do with providers in training—physicians, PAs, advanced practice nurses, or others. Do you have relationships on the education side of things? It sounds like you have a wonderful foundation of a network of both patients and providers. Would OFFER members consider becoming patient instructors who would talk about CFS to students in training? We've heard at our meetings since I've joined that there is a lot of bias in the provider community. Perhaps getting trainees to have a one-on-one discussion with a patient may be a way to begin to break down these biases.

Ms. Milne: That is one of our successful actions. After we print the provider brochure for the conference, for example, in addition to mailing them to doctors, we get them into the hands of patients so that they can take the brochure to their own primary care doctor and have the conversation that you are speaking about. Our education meetings are sometimes directed towards educating patients to better present their case to their doctor.

Dr. Bateman: We do have one board member (a nurse midwife who works at the university and has a daughter with CFS) who has taken it upon herself to set up speaking engagements for me and for other speakers. She has set up eight or 10 such engagements for me last year with providers in training.

Dr. Oleske: Let me take a second to introduce Dr. Hartz, who has now arrived and is the fifth new member of CFSAC.

Dr. Hartz: How do you help patients and physicians in remote areas that are far from Salt Lake?

Ms. Milne: That is part of our future focus. We have spent a lot of time in these last five years trying to build a relationship with the University of Utah in Salt Lake City. Since most of the people who receive our services are in Salt Lake County, that is where we have spent the most time. We do have an interest in penetrating the state and reaching those doctors. We know there are patients there because they come to our conferences.

Dr. Oleske introduced Dr. Joseph John (see page 23) who has worked at the VA Medical Center in Charleston, SC, for five years and in New Jersey for 10 years before that.

Dr. John: Linda's comments are reminiscent of what has gone on in New Jersey. The model that I can think of for what sounds like a great need to regionalize these activities—as has been done in Utah, New Jersey, and perhaps other states—is the Infectious Disease Society of America. The effort has been to create statewide societies. Those have been very successful and have resulted in annual statewide meetings. Without that kind of unifying, consistent regional representation that also serves as an outlet for provider education, it's very hard to get things moving in a state, find cohesion in how to educate patients, and establish continuity of care.

Dr. Oleske introduced the next speaker, Patricia Fennell, from Albany Health Management Associates, Inc., noting that the organization is dedicated to improving the quality of life of patients with any chronic illness. He added that CFS causes tremendous negative impacts patients' quality of life, and one reason why physicians need to pay attention to treatment symptoms—"which we sometimes don't do"—is to improve quality of life.

Patricia Fennell, *Albany Health Management Associates, Inc.*
Accompanying Document: *Quality of Life Considerations and Behavioral Health in CFS: Delivering Care in the New Chronic Illness Era*

Ms. Fennell presented at the OFFER conference several years ago in the area of chronic disease, sexuality, and the impact that it has on couples and families.

Her organization has been treating chronically ill patients since the late 1980s. It has conducted research and theory building, treated patients at the clinic, and handled comprehensive case management and policy work. She expressed hope that part of the message she's sending is that others might also be interested in the kind work done at the Albany clinic.

The environment has change enormously in the 20 years of treating CFS and FM patients, particularly in the last five years, said Ms. Fennell. There has been a paradigm shift in medicine from an acute care system, which is still out there, to a chronic illness system. The health thrust has shifted from narrowly focusing on one disease at a time such as arthritis, diabetes, and congestive heart. This is the larger environment that CFS patients are now part of. It stresses the necessity of chronic care models, and there are only a few of them out there besides our four-phase model. The paradigm shift has had good and bad impacts on CFS patients. It is beneficial for chronic illness to be a focus, but she wants to make sure that CFS patients aren't left behind.

Considerations when comparing chronic vs. acute illness:

- The different ways that chronic illness manifests in the body systems.
- How difficult chronic illness can be to measure and to treat.
- The impact of chronic illness on the physical, emotional, and social domains and how that impact persists over time and affects patient reporting, compliance, and coping.

It can be argued that medicine is having trouble adapting to the chronic model of care. Chronic patients are having trouble coping in an acute, episodic care delivery environment. How can we improve the tight coordination of care over multiple disciplines? Cindy [Bateman] mentioned that part of the success of her conference is that they do a multi-disciplinary

approach. When you talk about chronic illness, said Ms. Fennell, you really are talking about not only the physical aspects, but the psychological and social aspects and how they affect an entire family:

- Patients' needs vary over the duration of the illness.
- Patients suffer from social stigma, economic losses, and lack of knowledge and understanding about their conditions.
- Health care providers, patients, and family members become frustrated with the unpredictable symptoms and chronicity. One of the most important things that we can talk about is chronicity. People don't' get ill, get better, and go back to their pre-crisis life. By the very nature of chronicity, people go through cycles of relapse and remission. Providers see these relapses as failures. They are not failures; they are part of what occurs over time in chronic conditions.

Why the paradigm shift to chronic illness?

The increased prevalence of chronic illnesses in our culture. In 1995, *JAMA* (*Journal of the American Medical Association*) reported that half of the U.S. population had a chronic disease, not counting mental illnesses. CFS patients are part of this growing population.

We have an aging population. In Albany, NY, the average life span in 1922 was 53 years; now you will live to be in your late 70s/early 80s due to public health, antibiotics, and technological advances.

Four groups of chronically ill:

1. Traditional chronic (CFS, FM, multiple sclerosis, asthma, lupus).
2. Acute illness survivors (cancer, cardiovascular disease) with lingering symptoms who are being sent to us as CFS patients. We did not see these people 10 years ago.
3. "Persistent acute" (HIV/AIDS, stroke).
4. Natural consequences of aging.

CFS patients are going to be embedded in these larger groups with everybody competing for dollars for treatment.

Historically there has not been a lot of coordination across multiple settings, providers, and treatment in managed care. It's like the Wild West out there. There are all kinds of services being considered, but there is not a lot of coordination between them.

The Fennell Four Phase Treatment (FFPT) Approach

Research is being done on this model in a variety of places in the United States, including Cornell Medical Center, as well as in Belgium. Several things must be stressed about the philosophy of the Phase Approach:

We assume integration versus cure. We can't cure folks of a chronic illness. So how do we help them build a whole life? How do we work with their new norms so that they aren't a person attached to an illness, but a person who has an illness within the context of larger life?

We assume that the disease experience is traumatic in and of itself. Ms. Milne said that she has been asked over the years if CFS patients are abuse survivors who are now presenting with illness. She answers, simply no. The numbers of CFS people who have been treated in Albany over the years who also have histories of trauma are similar to cancer or AIDS patients. The types of trauma experienced by CFS patients are:

- Disease/syndrome trauma - the onset of the illness and its symptoms.
- Iatrogenic trauma - the experience that patients have in the health care system. The opportunity to be traumatized in the system increases over time because the patient is going in and out, over and over again. Clinician education becomes extremely important. I see patients who begin to avoid the medical system and avoid seeking care.
- Cultural trauma – How is the larger culture regarding CFS this week? Is it real or isn't it real? Right now attitudes are on an upswing with favorable articles. Those people around the patient can be vicariously traumatized. If the patient was the wage earner and he/she can longer go to work, families can lose their homes, jobs, and friends.
- Pre-morbid/co-morbid trauma – What were these patients experiencing before the onset? Were they already getting divorced, diagnosed with cancer, or experiencing the death of a loved one before they got CFS?

All of these things act concurrently on the patient's experience. Part of Albany's research is looking at particular social/cultural factors that impact the CFS patients' experience. Two of these are the cultural intolerance of suffering and the cultural intolerance of ambiguity. CFS involves many unknowns. People are going through cycles over and over and everyone around them—provider, family—gets to go on the ride with them.

The Four Phases of Chronic Change

The phases of change in a chronic disease are: crisis, stabilization, resolution, integration.

Each phase has three domains—the physical/behavioral, the psychological, and the social interactive.

When most patients come in for treatment, they are in the crisis or stabilization phase. Most patients loop between crisis and stabilization because they are always being encouraged to and want to return to the pre-crisis life. They must be assisted with moving on to resolution, otherwise they set up an ongoing cycle of relapse by doing too much and trying to use the same norms that would apply before they became ill.

Phase I – Trauma/Crisis

Physical/Behavioral – could have a rapid or slow onset, but in either case, patient ("Betty") begins to notice changes in the activities that she can perform physically (climbing stairs) and cognitively (cannot operate common machinery such as a television or telephone). She tries to cope until she is at the acute/emergency stage of this phase and can no longer escape the symptoms. She seeks care.

Psychological – Patients typically have a loss of psychological control—an ego loss. Everyone has a private and a public self. When people begin to experience the onset of an illness that is this significant, those two arenas begin to blend. Depending on the severity of

the onset, it can be a devastating experience triggering intrusive shame, self hatred, despair, shock, disorientation, and disassociation. It's typical for a patient to have a fear of others.

Social/Interactive – Those around the patient can experience shock, disbelief, or even revulsion, depending on the severity of the symptoms. They can be vicariously traumatized. How difficult this crisis phase can be depends on the family's maturation. Physicians in settings that limit the amount of time that can be spent talking to patients ask how they can treat CFS patients within such limits. The severity of this phase also depends on how much support or suspicion the patient and family receive from their peers, workplace, and clinicians. Belgian researchers report a crisis phase that is shorter by several months than that in the United States. Belgian patients did not have to negotiate the disability, work, and financial issues to the degree that U.S. patients must.

Phase II – Stabilization/Normalization Failure

Physical/Behavioral – The patient is not better, but is beginning to carve order out of chaos and understand what her symptoms are. She is beginning to understand how her disease is functioning (i.e., how often she can climb the stairs).

Psychological – Patients exhibit increased caution and secondary wounding. They begin to withdraw and search for others of like kind. As people stabilize, they begin to look for others who can give them information and understanding about their experience. There is some boundary confusion (person with a disease or disease with a person?) and service confusion, where patients are trying to work with their local clinician, but can't find appropriate services.

Social/Interactive – There is either increased cooperation or conflict. It is not unusual for a spouse to declare, "I did not sign up for this." Ms. Fennell explained that we are not trained as a culture to think that we are going to get chronically ill. She has yet to see a patient go through this process and not lose someone who is significant to her. The kind of divisiveness that this creates in families is huge and expensive (lost wages, divorce, etc.). As a result, patients try very hard to be who they used to be, often resulting in normalization failure.

Phase III – Resolution

Physical/Behavioral – There is an understanding that relapse is part of how chronic disease functions.

Psychological - There is imposed change that people do not want to make. To recognize that they can't have their pre-crisis life takes a huge psychological jump. It is in this phase that a true grief reaction sets in. People in the crisis phase are frightened, depressed, or angry. In the resolution phase, they begin to grieve for their pre-crisis self. This almost always has to be done with assistance. This is where people are most at risk to commit suicide and abuse substances to cope. To recognize the level of change that is required is huge. If people are to shift, they have to develop meaning about their suffering.

It is important both medically and emotionally to match interventions with the phase and stage in which they will be most effective. At Phase III, when people are dealing with grief issues at a much higher level, they need different types of techniques. What a patient looks like in year one and what she looks like in year eight is not the same. The people around her do not look the same.

Social/ Interactive – We see patients engage in a whole variety of things, such as becoming invested in doing different kinds of advocacy work. That is one choice for people. They may engage in different types of role experimentation, including retooling for a different job. This is where there occurs a reintegration or permanent loss of supporters. Some of the people who patients reached out to in Phase II become integrated into their lives.

Phase IV – Integration

Physical/Behavioral – Patients have an expectation of relapse and remission.

Psychological – Patients have developed a new role and identity.

Social/Interactive – There is new integration of supporters.

People do not go through the phases in this model once. It functions like a cognitive map. There is not a lot in the media about chronic illness and what people can expect over time. Part of what we teach is that if you go through the phases once and you get assistance and you do it successfully, you're better prepared for what comes next, whether it's a relapse, a different disease experience, or a normal developmental stage of life.

Traumagenic Effects

Intolerance of chronic vs. acute syndromes:

The dynamics of intolerance include pressure for a "cure"/normalization, lack of treatment models, frustration conveyed by those trying to provide treatment, punishment for healthy self care and rewards for unhealthy self care.

The effects of intolerance include normalization failure, increased salience of abuse issues, avoidance of intimacy, and social withdrawal. Ms. Fennell said she would like to see the U.S. reach the point where CFS patients don't have to pretend they don't have CFS in public or lie about having CFS so that they don't experience stigmatization.

Treatment

The Albany clinic works hard to match intervention to phase, and sets treatment goals at each phase. Case management is very specific. Evaluation includes medical protocols, coordination with clinicians, psychological support and intervention, self management, and disability issues. Albany also trains medical professionals of all types and would like to train more.

Each phase has a clinical goal and a case management goal:

Phase I

Clinical goal - Trauma and crisis management—get the patient contained through BATOS so that the disease process doesn't get any worse:

Bond - The type of bonding required from a psychological perspective is difficult when the patient is covered by health insurance that requires that this occurs in nine visits or less.
Affirm – Staff must affirm a patient's experience.
Teach grief response – Patients learn how grief and the trauma reaction affect them and are taught the chronic disease phases.
Observe - Patients learn how to observe their behavior so they can learn how to function differently.
Safety Plan – Staff assists patients in establishing very specific safety plans.

Case management goal - Establish a case management focus. Restructure daily activities, conduct family case and health care system management, and develop training and interventions for the workplace.

Phase II

Clinical goal – These patients have to learn how to be different people and that's a big job. The goal is stabilization by teaching patients CDIN:

Collect data.
Differentiate the psychological from the physical and the social. Specifically describe the condition rather than using vague descriptions such as "I feel bad."
Insight development in which patients learn their own process physically and psychologically.
Norms/Goals – Patients develop new norms and goals.

Case management goal: Data collection and activity restructuring. Also included are helping patients develop new norms, case management of family and health care, and clinician advocacy.

Phase III

Clinical goals – Help patients develop meaning about this experience and construct a new self through GMR:

Grieve - Human beings need a story to help explain why they've gone through this trauma and why they should bother to continue to so, or people just don't want to do it. This is part of the necessity of grieving and differentiating this from the clinical issues of depression.
Maintain – Staff work to help patients maintain their insight.
Reframe – Staff helps patients reframe their experience into how to play a poor hand well.

Case management goal – Self management skill development is key. Patients need to learn how to monitor their own activities—how they walk, how are they eating, what their symptoms are. Patients also get help with medical coordination and learning how to be their own advocates.

Phase IV

Clinical goal – Integration. "It is what it is."

Case management goal – Facilitate patients learning how to do their own self management.

Committee Members Q&A

Dr. Oleske: What you have presented is a comprehensive way of managing someone through a chronic illness. How is that paid for? How do people access that?

Ms. Fennell: Some of the services are paid for through insurance as a psychological service. We've have varying success getting payment for case management. The case management that patients could have done in conjunction with their primary care physician years ago just isn't available anymore. These cases absolutely need to be case managed, and that's not paid for, so that is something that we would like to see changed.

Dr. Jason: Patients frequently mention that they have a very short time when they see their medical practitioner. Often medical practitioners talk about getting punished for spending more time with patients who have complex issues. How does one deal with those system issues that now affect patients with ME/CFS that allow them to have the time to go through the type of treatment and management that you're talking about? For cancer and MS and some other illnesses, you do have centers that you can go to get that kind of comprehensive treatment. Is that something that you think might be needed in this field?

Ms. Fennell: The truth is that almost all of the chronic diseases are having the same struggle, and part of my concern is that CFS doesn't get lost in that morass. I think we're looking at a time where the whole healthcare system is struggling with being retooled, moving from an acute care system to a chronic care system. Currently, it's organizations like mine that are trying to provide a stop-gap measure in case management to work with the physicians and clinicians, because the system does not exist. Part of what we're trying to do is create a discipline that works along side of the primary care providers in clinical case management.

Mr. Newfield: At the OFFER conference, we heard a doctor from Sweden talking about being able to go out on disability ("burn out"), and how in the United States, they do not permit going out for disability from burnout. They would take the position that while you can't do that job in that particular place, you can do some job, and therefore wouldn't qualify. Is there any data from Belgium that we can look at and use to help advocate? Perhaps they can make a presentation to us.

Ms. Fennell: That would be a good question to pose to those colleagues, and I can share that with you after the fact.

Dr. Papernik: When the patient is being seen for the first time clinically, he is looking for a diagnosis. It is not going to be well received if I say, "I think you have a chronic disease. I want you to see a psychologist or psychiatrist to go through these steps to learn how to deal with your illness."

Ms. Fennell: You make a very interesting point, that when someone first comes to you and they may in fact have a chronic illness, but you have no idea yet, that would not be the time to introduce them to this model.

Dr. Papernik: That's my point, that this is a model that needs to be used once a diagnosis has been made, knowing that what lies ahead is these stages.

Ms. Fennell: It could be a lengthy process of diagnosis. You may have to put them through months of testing. You might have a diagnosis that you start with; you may need to reframe it as time goes by. I would advise folks to consider starting this process if you're several months in. If someone has been flailing around with their symptoms for five or six months, they need to begin to have some intervention on this level.

Dr. Oleske: Thank you for a wonderful presentation…I have asked Dr. Joseph John to come as my guest. He is an outstanding clinician. He and I wrote the New Jersey *Management of Chronic Fatigue Syndrome Manual* that has been adopted in Vermont and some other states. My concern, and one of the things that I hope we accomplish as a panel, is to change the paradigm so that patients with CFS receive treatment for their symptoms. What I find, unfortunately, is that a CFS patient can have all of the symptoms of a seasonal allergy, but they are being ignored because they have a chronic diagnosis.

Update on CFS Treatment

Dr. Joseph John, Jr., *Veterans Administration Medical Center, Charleston, SC*

Dr. John provided a review of where the field has been over the last several years rather than just a focus on treatment. He commended Pat Fennell for presenting a truly holistic framework in which to start thinking about teamwork in treating CFS.

He thanked CFSAC members for the data that they have provided and produced over the years in their studies. The term "fatigue" has some interesting historical frameworks, he continued. It probably had its origins in the industrial revolution, since it was not a legacy of human behavior coming up through that time. The term did not start to pervade the literature until the 19th century. In Japan the condition is called a cytokine syndrome, because it suggests a mechanistic basis.

Diagnosis

Dr. John said that he guides patients through a thorough self-inventory before deciding on their treatment. He may ask a patient to construct a graph where 10 is good and zero is bad. There are other rating systems, including a quantitative one that Nancy Klimas and some of her colleagues have been working with internationally. Some of the multi-dimensional fatigue inventories could also work well, he said. The SF-36 Form is something that could be used more commonly than is the case, but it is very hard to do in a 15-minute visit with a busy primary care practitioner. Dr. John consults a flow chart in his office that depicts the steps toward diagnosis and checks them off as he goes. He added that it is valuable to have individual appointments focusing on different aspects of diagnosis.

Dr. John echoed Dr. Papernik's point that a lot of differential diagnoses have to be ruled out, and this takes time. Dr. John said that for the last decade he has been attracted to the idea that there are some specific anti-viral mechanisms available to cells that have to be overcome in viral illnesses that use host machinery as a basis of their pathogenicity. This idea of a channelopathy gives a totality of diagnoses to explain the expansive symptomatology that CFS patients have, he said. A patient could have defective anti-viral machinery that could relate to

membrane destability. These ideas assist in understanding the dysfunction of amino acid building blocks and the type of pain symptoms that they might relate to.

When faced with colleagues who say, “This is not a disease,” Dr. John’s response is, “Do you believe in congestive heart failure?” which is simply a gross syndrome of cardiac dysfunction. CFS is a set of criteria that fit a large number of patients’ illness and Dr. John said that he carefully categorizes them not only for therapy reasons, but for disability and psychological rehabilitation.

There is fascinating epidemiology for this disease, he continued. Data from a Dutch study of French and Belgian soldiers returning from Cambodia with CFS-type symptoms show 19% recovery, 20% improvement, and 57% with delayed and continuing complaints.

There are other data generated by the Persian Gulf War, said Dr. John, but there has not been a good follow up on the clinical symptomatology. When a patient says that “It all started when that horrible hornet bit me back in ’95 and I never got better,” how does one put that into a whole framework? But it must be done. There are other more serious, provable surrogates of initiating disease like toxoplasmosis or HHV6. Dr. John said that he likes the idea that predisposing factors imply some genetic basis—that there are initial environmental factors that patients come into contact with and respond differently to in terms of complaints. So there are predisposing factors, initiating factors that feed into patient complaints, then perpetuating factors.

One question is, how much lab work must be done for a CFS diagnosis? In this age of HIV and retroviral illness, we can start to talk about cellular dysfunction. One constant construct in this disease has been NK cell decrement in number and function. That has been a valuable place to go if patient’s insurance will pay for it and a physician can get a lab to do it. There are several HHV6 labs that have shown a large overlap for this illness. Dr. John suggested that as more is learned about HHV8 in interaction with HIV, it will open some new doors for more study of HHV6.

He added that researchers are also advancing towards more understanding of the pathophysiology through imaging. Japanese colleagues presented broad-based brain imaging findings at the 2005 CFS conference that reflected back to earlier studies suggesting deep changes in white matter. There has been a legacy of dysfunctional anti-viral machinery.

Dr. John reiterated that there may be some kind of final common pathway for channel dysfunction, which is at the basis of many illnesses today. The bottom line: There are probably multiple viruses involved in this disease, there is certainly a genetic predisposition, and there’s a broad-based cellular response to whatever physical or microbiological trauma has evidenced. Work coming out of CDC on gene expression suggests abnormalities in down regulation of sets of genes in transcription cell cycle and less up regulation in areas of other metabolic functions.

Dr. John offered other thoughts on diagnosis including:

- The importance of understanding how difficult it is in the early part of these illnesses to categorize the widespread set of symptoms.
- The neglect over the last few years of the role of headache in this illness even though it poses a major problem.

- The necessity of a few more tests in addition to the standard lab work mentioned in the *ACP Observer*. He noted that there is a debate among endocrinologists over what one does to work up the pituitary adrenal axis and whether a random cortisol is adequate. A fairly normal-to-high-normal cortisol can at least indicate that the patient does not have Addison's Disease. The debate emphasizes the importance of educating providers that this is a multi-system, multi-functional disease.

Treatment

Dr. John addressed the role in disease management of less well proven treatments like acupuncture and psychotherapy, noting that he liked how the *Observer* article handled herbal and over-the-counter therapies by saying that they do work for some patients. He said that there is hardly an acknowledgement of that in the literature. Dr. John noted, however, that patients do not always have access to recommended treatments like psychotherapy. There are only three psychotherapists in Charleston, for example, and it's a pretty big town. Patients may wait months to line up their treatments, referring to Ms. Fennell's presentation as illustrating the necessary level of sophistication and organization for doing so.

As far as pharmacological therapy, Dr. John said that many options are at a physician's disposal. There is ampligen therapy going on, and while researchers may not have totally discarded the micro plasma hypothesis, there are many groups of drug classes available and newer agents coming onboard. One generating excitement is cyclovere, particularly as it would be a herpes virus group stabilizer. Also being studied are anti-dementia drugs and those used for bipolar and other chronic brain diseases. There also may be a role for magnetic therapy, including a way to titrate a diagnosis with magnets.

Dr John cautioned, however, that working with some of the newer stimulants coming on the market may be problematic because the long-term affects are unknown. He also noted that bipolar disease is becoming much more prominent in the consciousness of clinicians who treat CFS patients, particularly as it affects their psychological adjustment. A CFS patient without bipolar disease can come to a new self-realization in a way that bipolar patients are blocked from.

Dr. John noted other aspects of treating CFS including:

- Disability considerations are paramount. Patients need to understand that they will have a physician's patience and assistance in finding good lawyers who will help them.

- A holistic approach to CFS would include things like the Albany management system, which recognizes that the disease occurs within a social/psychological environment.

- An Australian study shows that CFS patients in a graded exercise group have an increase in power output. CFS patients need a certain amount of rest, but it has been shown that both cognitive therapy and exercise therapy are beneficial in their regimen.

Dr. John concluded with his hopes for the future:

- Genomics will open some doors so that the social medicine world will accept CFS.

- As immune and endocrine are function better understood, doctors will know when those systems are bedeviled by a specific triggering agent, be it warfare combat, infectious agents, or personal psychological trauma.

One of the challenges of CFSAC and a basis for comprehensive and multi-center studies is invoking the practicing community into taking care of CFS and studying that is best done. The medical investigative challenge remains.

Committee Members Q&A

Dr. Oleske: You, Ms. Fennell and others are advocating a comprehensive approach using different disciplines and good rehabilitation including medication. The thing that troubles me is that one of your clinics was closed for financial reasons. Can you talk about what happened what it implies for other facilities and a new generation of medical people? Are they going to be attracted to a field that has such economic consequences?

Dr. John: It's very tough. In a nutshell, there's got to be departmental support from the top. If you try to initiate these kinds of efforts from the bottom, you're crawling uphill. We all know what the chairmen of these academic departments are like today. They need to be handed a workable business plan that is viable. How few of our junior colleagues can do that? They're not raised as business people, but they need to collaborate more with the business people. Another way to garner support is to avoid being seen as working in your own enclave, because that makes you vulnerable. The CFS activity in my facility was vulnerable to closing because it wasn't intertwined with endocrine, pediatrics, or even infectious diseases.

Dr. Klimas: I had similar financial issues with my own department. When I presented it to my chairman as a community service for an unmet need of the community, I hit a different tack. A medical school is one place to set up these center models, and part of medical school funding is often meeting the needs of the community.

Dr. Oleske: One of the recommendations that CFSAC has made already is the concept of clinical centers of excellence and clinical trials located regionally.

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

Dr. Oleske: As a pediatric immunologist, I only have the greatest admiration for Dr. Krensky's achievements in transplant immunology and taking care of children. He's going to be talking about the Roadmap Initiative. I hope we realize what a wonderful, generous opportunity this is from Dr. Krensky to find out how we could have CFS placed on that Roadmap.

Update from NIH – Roadmap Initiative

Dr. Alan Krensky, Director Designee, *Office of Portfolio Analysis and Strategic Initiatives (OPASI), National Institutes of Health*
Shelagh Galligan Professor, *Stanford University*
Accompanying Document: *The Office of Portfolio Analysis and Strategic Initiatives*

Dr. Krensky noted that he will formally start in his job as the new Deputy Director of NIH and Director of OPASI on July 8. He explained that the NIH Roadmap Initiative will reside in the brand new office called OPASI, and that there is both good news and bad news for CFSAC under the OPASI approach.

The first omnibus reauthorization of the NIH in 14 years just occurred. Congress passed it in December 2006 and President Bush signed it into law in January 2007. The NIH Reform Act of 2006:

- Establishes a Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI).
- Establishes use of a Common Fund to support trans-NIH research.
- Creates a Council of Councils to guide trans-NIH priorities.
- Establishes a Scientific Management Review Board (SMRB) overseen by Secretary that evaluates NIH organizational structures and authorities. This group will meet regularly and have the opportunity every seven years to recommend improvements in the NIH structure.
- Initiates a public process to review organizational changes. There will be a public process accompanying any recommended changes.

OPASI's Mission

- To provide NIH Institutes and Centers with the methods, tools, and information necessary to improve the management of the large and complex scientific portfolios.
- To identify—in concert with multiple inputs—important areas of emerging scientific opportunities or rising public health challenges.
- To help accelerate investments in these areas, focusing on those involving multiple Institutes and Centers (ICs) rather than those within the purview of one or two.
- To coordinate and make more effective use of NIH-wide evaluation processes.

Structure of OPASI

- The OPASI Director reports directly to the NIH Director and sits in on all major decision-making processes for the agency.
- The NIH Steering Committee, or OPASI Working Group, will be made up of IC Directors who will advise the OPASI Director.

There are three divisions within OPASI:

Division of Resource Development and Analysis includes portfolio analysis, which has two major pieces—

- Develop new tools and information systems to better track NIH funding.
- Determine whether resources are being spent in the context of health needs and burden of illness. Economists, epidemiologists, and sociologists will help determine whether NIH is effectively addressing the public health of the American people.

Division of Strategic Coordination, which includes the NIH Roadmap, will also deal more broadly with strategic coordination of the 27 ICs.

Division of Evaluation and Systemic Assessments will conduct governmentally required evaluation procedures assigned as part of NIH's responsibility. In addition, the division will launch trans-NIH initiatives that use state-of-the-art techniques to conduct effective evaluations of all NIH programs.

OPASI was created so that portfolio analyses, strategic initiatives, and evaluation all interact and inform each other. At the same time, OPASI is a service organization dealing with the 27 ICs and how they should interact in cross-cutting, coordinated ways. It is not going to be a place with line items for particular disease like you would find in a Center. Many advocates believe that their illness is not represented at NIH and are hoping that OPASI is a place for such representation. This is not the way that the process works.

The OPASI **Common Fund** will be contributed to by the various ICs, but for the first year, Congress provided $480 million as a line item in the NIH budget. The Common Fund will be used specifically to fund Roadmap Initiatives.

A Roadmap Initiative must demonstrate:

- High potential to transform how biomedical and/or behavioral research will be conducted.
- Synergistic promotion and advancement of the individual missions of the ICs to benefit health.
- Applicability to issues beyond the scope of any one or small number of ICs.
- Likelihood that no other entity is able or likely to perform the work.
- A public health benefit of having the results of the research in the public domain.

NIH goes through the process of choosing initiatives every two to three years. Under the current timeline:

- There were scientific consultation meetings in early 2006 within and outside of NIH that included a variety of people from industry, academics, and the Council of Public Representatives.
- By summer 2006, a variety of ideas were being culled by the NIH staff. Over 350 opportunities were gathered in a huge binder that went out for review and discussion.
- On January 4 2007, Dr. Krensky conducted a full-day operational event where all ICs got discussed the proposals and prioritized them to pick areas for the next round of funding.

Of the $480 million, there is only $30 million available for new projects. Areas have been selected for discussion. They are not yet RFAs (requests for applications). On Friday, May 18, the IC Directors will vote on areas that warrant further evaluation before RFAs are developed in the fall.

Although nothing in the Roadmap is disease-specific, all areas have implications relevant to CFSAC and the committee should be excited at the tremendous potential. CFS is one of the

diseases for which the Roadmap topics could have huge implications. These topics have not been finally selected and they may not all make it into the Roadmap this year—

Potential Roadmap topics under discussion:

The microbiome is an exciting concept that has come up over the last couple of years. Probably the most provocative piece of data is that researchers can take the microbes from the gut of one animal, put them in another animal, and have that second creature go from being fat to thin. The human body has more microbial cells than human cells. NIH proposes to start sequencing these microbes, defining the panoply of microbes that inhabit the human body. A lot of work has been done in the gut, but every orifice of the body has a group of microbes. These are highly likely to tell us about a number of diseases, including CFS.

Inflammation as a common mechanism of disease. The immune system underlies the majority of human diseases in one way or another.

Protein capture agents and proteomics. The genome project revealed a lot about genes, but researchers are just beginning to learn about proteins. One gene can give rise to many proteins. Because proteins are much more diverse than the genes, proteomics is an area of great importance.

Standardization of human disease phenotypes. Not everyone does a blood pressure test the same way, meaning that when these blood pressures are reported in studies, the results are not standard. This is mundane but important if researchers are talking to each other about data. At the other extreme of these phenotypes—and I'll use the immune system as an example—no one has discovered a biomarker for CFS. We really don't even have biomarkers to measure how well the immune system is working.

Epigenetics. The genes exist and they code for proteins, but epigenetics—other enzymatic effects—affect the genome in which genes are turned on and turned off. A lot of work has been done in this area, but researchers have come up against many roadblocks. New technologies are needed to understand how genes are turned on or turn off.

OPASI is not just about the Roadmap, but other trans-NIH cross-cutting areas. The most important areas at this point include:

Obesity, which is the biggest public health problem in this country. Remarkably little is understood about it, but it is an important behavioral target. It's an area to which NIH has paid relatively little attention. There is a fledgling obesity initiative, but it is underpowered for what it has to do for the American people, said Dr. Krensky.

Neuroscience Blueprint runs a close second to obesity in priority. NIH has seven core neuroscience Institutes and 17 involved in what is called the Neuroscience Blueprint. The potential for big, bold, new views of how to deal with things like pain or chronic fatigue really lies in this constellation of interaction dealing with a variety of disorders, said Dr. Krensky.

Regenerative medicine has become a catch word for everything from battlefield wounds in Iraq to the idea of taking fat cells from your body and making new brain, kidney, or liver cells

out of it. Regenerative medicine is a broad area and a real opportunity for all the agencies within the department to work together.

Informatics (information systems) underlies everything. This goes from bioinformatics, which support things like microarrays, to medical informatics and how records are moved from paper to new interconnected information systems that help provide up-to-the-minute bedside care up-to-the-minute.

Pharmacogenomics is an area that almost every Institute within the NIH is working on. There is a lot of potential for collaboration when looking at how drugs relate to the genes of each individual.

Health disparities include those associated with race, sex, and socioeconomic status, the last of which is one of the biggest health issues in this country at this time.

A children's health initiative(?) This is a less developed concept than the others. Congress has funded a National Children's Study that has just started and is looking a genetics and environment and looking in a prospective way. There are several institutes within NIH that address children, but they don't really work together as a cohesive whole.

How will OPASI likely affect trans-disciplinary research?

- Roadmap Initiatives, by their nature, will be more likely to cross disciplinary and organizational boundaries. They will tend toward "Big Science" with implications for many different diseases.
- They'll tend to be larger infrastructure-type projects with open access to multiple disciplines and research areas.
- Portfolio analysis tools will be used to evaluate NIH investments to promote connections and avoid duplication of effort.

Factors for success

- **Science First** –pushing the edge to promote research that isn't being done elsewhere.
- **Planning based on evidence** that the projects chosen will bear fruit, although there will also be venture element.
- **Maintaining transparency** so that the community outside NIH understands what is going on at each level.
- **Communicating plans** – The CFSAC presentation has been part of this communication, said Dr. Krensky, and he called on members to provide feedback.
- **Managing change** – OPASI is geared toward trans-NIH initiatives and collaboration. The Common Fund is brand new and a very small part of the NIH budget. OPASI's success will be measured by its ability to fill research gaps, alleviate redundancies, and add value to the strategic planning of the portfolio of the largest biomedical research institution in the world.

Committee Member Q&A

Dr. Glaser: You can put as much money as you want into programs doing multi-disciplinary research, but if you don't have people on study sections who understand that, you're going to

have a problem. That's what came out of a meeting that took place a few weeks ago at NIH that examined the study section program. There was consensus that the general structure of study sections is fine. The problem is that the membership of those committees wasn't able to do multi-disciplinary reviews, which results in good ideas not being funded, including those related to CFS. What is your comment about that?

Dr. Krensky: You're right on in all of this. It is essential to the NIH structure that peer review and program decisions are kept separate. There's a firewall there and that will be maintained. That being said, peer review is on hard times for several reasons. Everyone agrees that peer review is the best thing that we can do. But with the doubling of the NIH budget, there was a doubling of the number of grant applications. Study sections that had 20 people now have 50. Study sections that had the same senior people consistently conducting reviews now have ad hoc members.

There is a blue ribbon committee as well as an internal committee generating ideas to solve the problem. One idea is to review proposals based on the peer review journal model where a large group of people do the initial reviewing, then feed into a smaller group of senior experts. NIH will conduct pilots before changing its study section system. We realize that our current system encourages reviewers to make "safe" choices.

Dr. Jason: When you have 15 or 20 people on a review panel, there's no way that they're going to have the expertise for 100 areas, and I think that's the basic problem. The review journal approach is a brilliant idea. I had a question on the $30 million and what percentiles are going to be available for the number of proposals coming in.

There is also a larger issue: CFSAC is a good fit with what you're talking about. We are multi-disciplinary. The things we're interested in are broad and affect multiple diseases that we have expertise in. One of the problems is generating enough study subjects to look at the subtypes and small phenomena that we're interested in. Is it possible with some of these Roadmap Initiatives for collaboration across sites in different locations in the country to get what we need for our research?

Dr. Krensky: There will ultimately be 60 translational science groups across the country based on a clinical trial infrastructure. They will interact with each other and they will not be disease specific. When they set up genomic genetics, pharmacogenomics, proteomics, etc., those will be available as an infrastructure to every disease group. OPASI and DPCPSI are going to try to build things that everyone can use.

My take-home message is that OPASI, DPCPSI, and the Roadmap will have great implications for CFS. The goal is to try to get the neuroscience blueprint to work together. Neuro, immuno, endocrine…we call these different systems and they're really not. The human body works as an integral whole, and I think CFS fits into that. CFS is a syndrome just as most of the diseases we deal with are syndromes. Heart, diabetes, and cancer are not one disease. What we're learning in the genomic era is how to subdivide these diseases. That's what's going to happen with CFS as well.

The real answer to finding therapies and the biomarkers to diagnose the disease is to start subdividing it. OPASI is fostering a new kind of research different from the hypothesis-driven research that NIH was built upon. The diabetologists might find the cure for cancer, and the cancer doctors may find the cure for CFS. These are all overlapping. That's the reality of the

biology. It's a change for NIH. I'm not saying do away with disease specificity, but we have to work together because there is a lot more that we can get with these cross-cutting ways.

Dr. Klimas: The Office on Women's Health put out an RFA on CFS and got four or five times the proposals expected in an area desperate for new people. How is OPASI going to affect the Office of Women's Health. Are they going to be able to get money through that mechanism?

Dr. Krensky: Within DPCPSI, all of the offices of the director are put together. There are no announcements yet about what it's going to look like, but included in those are OPASI and the other programmatic offices like Behavior, Women's Health, AIDS, and the Office of Disease Prevention, which includes rare diseases and dietary supplements. These are areas that didn't fit into any other group and went into the Office of the Director. But they're all inherently trans-NIH and cross-cutting. Congress does not want any more programmatic offices just like it doesn't want any more Institutes and Centers. Any new areas to be studied will be through functional integration, not structural.

I think that the mechanism that was used by Women's Health to specifically fund CFS is an example of the system working really well. The biggest issue for Women's Health and all of NIH right now is that we've had a shrinking budget in real terms. It is difficult to develop new programs or add new programs when your budget is shrinking. There are lots of really good new ideas—more than ever out there—but we need the money to implement them. I think that Women's Health, if asked, would tell you that they're happy with how the RFA but their reality is that they have less money than they had last year.

I think that in a shrinking budget, all fields are at relative risk. Some already have a lot of money and others don't. The NIH is ready to have a huge impact on public health. This new office is designed for that. This is a new way to approach things, and with new moneys going forward, I think there will be a huge impact, but the NIH budget, since the doubling, has gone down in a dramatic way. I think we've never had an opportunity to do more for CFS, but money is the oil that makes the machine run.

Dr. Oleske: In this trans-NIH program, how is the individual investigator-driven proposal going to be treated? It's hard for an individual investigator to write a proposal that encompasses this trans-NIH potential.

Dr. Krensky: Investigator-initiated awards are the gold standard of the NIH. Everyone thinks that's our priority. Within the Roadmap in particular, we may build the infrastructure, but it will be the individual investigator who proposes to study CFS and the proteomics core. The Roadmap has its special review groups and they are all told that we're looking for something outside the box and trans-NIH. Under our current system, people tend to avoid pushing the envelope. Peer review often goes for the common denominator. One of the first things that OPASI is going to do is have a session about innovation.

Dr. Snell: What I'm hearing is that if we want to tap into this fund, we need to rethink CFS and look at it somewhat differently. For example, we do a lot of research with exercise. Typically people with CFS don't exercise. So if we approach it from the perspective of obesity, use CFS as an example of inactivity, and look at why people may or may not become obese in association with CFS, that would be looked upon more favorably than a pure CFS approach?

Dr. Krensky: That's my message. I think that's a good way to go, but I'm saying that it's not mutually exclusive. Someone can still submit proposals to disease-specific areas. But my own personal bias and what I think OPASI is about is this bigger way of looking at things. There almost isn't a disease that can't be covered in the Roadmap. It really is a very powerful way to jumpstart science, this collaboration.

[Dr. Oleske called a break for lunch.]

Update from CDC – CFS & CDC Organizational Structure

Dr. Joanne Cono (via remote telephone hookup)
Dr. William Reeves, Chief, *Viral Exanthems and Herpesvirus Branch*
National Center for Infectious Diseases
Accompanying Document: *CDC CFS Program Update May 2007*

Dr. Reeves

I am reviewing the CDC CFS program in general to set the stage for my colleagues. Dr. Cono will then speak on the organizational status of the CFS program at CDC and Dr. Fridinger will talk about the public awareness campaign.

We look upon CFS as a complex illness, not as a disease. Diabetes is a disease with metabolic pathways involved. CFS is an illness from which various diseases spring. Ms. Fennell talked about 21st century chronic illness. We're looking upon CFS as a model of 21st century illness in terms of treatment and pathophysiology:

- CFS represents alterations in complex systems of homeostasis. It is an entire body illness.
- We're not going to see a single mutation or environmental factor that causes CFS.
- Rather, CFS and all complex illnesses arise from genetic interactions, epigenetic interactions, what you have experienced in the environment, and the way that you've reacted to it. It reflects your genetics and everything that has happened to you in the past and present.
- Complex diseases like CFS require multidisciplinary approaches.
- As discussed in the Roadmap Initiative, understanding CFS may help us understand common pathways for other complex illnesses such as post-vaccination or post-Katrina health issues.

What is the objective of CDC's CFS research program? To devise control and prevention strategies for CFS. Prevention right now is out of the question because we don't know the cause and metabolic pathways. Control, on a public health basis, would be decreasing the morbidity imposed by CFS on the population. This could be measured by:

- Prevalence – reducing the number of people who have CFS.
- Duration of illness – Most people with CFS seeing physicians have been sick for five years on average. If that could be cut, it would be an important measurable outcome.

- Impairment – We know that people with CFS are as impaired as people with AIDS, breast cancer, and end-stage renal disease. CFS patients don't have death as an outcome, but on a daily basis, that's how impaired they are. Control would reduce measurable impairment.
- Economic impact – The average family in which someone has CFS forgoes $20,000 in annual earnings. That's half the median income in the United States.

How do we do implement the CFS control strategy? What does control consist of? Using a simple logic model, you have sick people within the population, some of whom have CFS. You get CFS patients into some sort of intervention or treatment, and that intervention or treatment has measurable outcomes on a population basis and on an individual basis. Obviously the intervention must be based on a lot of knowledge. People need to be able to evaluate and diagnose CFS [right now there are no diagnostic markers] and they need appropriate management strategies. The CDC research program tries to work at diagnosis and management through:

- **Surveillance studies of defined populations.** When you look at the population, you can determine how many people have CFS (prevalence), you can look at new cases (incidence) and you can look at demographics (more prevalent among women/adults). Surveillance also looks at factors such as clinical attributes, risk factors, clinical course, and economics.
- **Clinical studies** that look at people in detail in a controlled clinical setting. This allows study of clinical attributes in more detail as well as risk factors, pathophysiology, and biomarkers.
- **Detailed lab studies** that delve even further into clinical attributes, risk factors, pathophysiology, and biomarkers.

Population-based studies are important because clinical studies only look at those people who visit the facility. Studying volunteers presents similar limitations. Volunteers "are generally those who run to the front" and are not like everybody else. If you want to know about an illness like CFS, you need to look at the population with a study in which everybody in the population has a known chance of being sampled.

How might we study CFS so that we can generalize it to the United States? Dr. Jason's group studied CFS in Chicago and the CDC studied it in Wichita. We had some differences in what we saw and we couldn't be certain why those occurred.

The CDC is currently conducting a study in Georgia that includes the Atlanta/Macon metro area and the surrounding 12 rural counties. We have done a random survey of people in those areas through phoning 10,000 households:

- We questioned a respondent in each household about everybody in the household. We are looking for people who are unwell (anything that would go with CFS – fatigue, cognitive difficulty, pain, insomnia).
- We then talked over the phone to the unwell for 45 minutes.
- About 90 percent of the houses answered the phone. Seventy to eighty percent finish the interview.
- Interviewees are brought into a clinic for a one-day evaluation.

Population Surveillance Results:

- A **prevalence** paper will be published in *Population Health Metrics* in early June. Prevalence rates are quite different than we thought they would be. There are no differences in the metropolitan urban and rural populations. Women continue to have a much higher prevalence than men. There is some evidence that this may reflect gender rather than sex.
- We have a **clinical attributes** manuscript in review indicating involvement of the cerebral frontal cortex and basal parts of the brain in cognitive function.
- We have found early childhood abuse to be a big **risk factor**.
- **Clinical course** is going to require a follow-up.
- We're in the midst of an **economics** evaluation.
- We're looking at **access/utilization of health care** and **biomarkers**. Both are works in progress, but it's clear that there is a blunted diurnal cortisol response.

We have finished the baseline. As soon as the Office of Management and Budget (OMB) approves it—hopefully in August or September—we will do the first follow-up of this to look for incidence cases, look at the clinical course, and do a CFS patient registry.

We are in the middle of the population survey, we know the occurrence of CFS in the population, we have gotten most providers (physicians, nurse practitioners, PAs, chiropractors, massage therapists, school nurses) to refer us all of their patients so that we can look at those people getting healthcare compared to the population.

Emory University is interested in treatment trials and setting up a CFS center of excellence.

We have looked at a fair number of providers for their knowledge, attitudes and beliefs (KAB) concerning CFS as well as the KAB of the general public and patients. Surveillance studies provide a lot of information, but the data they provide are limited to how much time you can spend with a large number of patients. Among the data gathered is that 48 percent of people going through the clinics who would meet the criteria for CFS had a readily diagnosable and treatable medical or psychiatric condition such as thyroid disease, diabetes, substance abuse, etc.

In-Hospital Clinical Study of CFS

Our in-hospital case control study will bring in 60 patients with CFS for three days to Emory Hospital. On the first day, we will conduct functional magnetic resonance imaging during a cognitive task. The second day, we will conduct functional magnetic resonance imaging looking for pathways involved during a cognitive stressor while drawing blood every 15 minutes. The third day, we will shut down the HPA axis with dexamethasone and give patients a challenge with corticotropic releasing hormone to see their various stress responses. This will also be monitored with 15-minute blood samples.

What we can measure in the laboratory is the genetics. We know the genetics of the population in Georgia that we've surveyed. We can consider epigenetics (modifications in genomes due to life experiences) by looking at messenger RNA and we can look at the various proteins.

Laboratory Study of CFS

Everything we do involves lab studies. Blood is being studied from both patients who come into our clinic and those from the in-hospital study. We can look for risk factors, biomarkers, and pathophysiology:

Plasma, serum, and PBMCs (peripheral blood mononuclear cell) allow measurement of exposure to infectious agents, proteins, cytokine responses, and immune function. Saliva lets you measure the cortisol (physiological stress) response. Researchers then have to put it all together. We know very clearly now that CFS is a mind/body type illness and involves the hypothalamic/pituitary/adrenal axis—we have a million data points on every patient. This comes back to the Roadmap Initiative. You have to put this together in a clinical context and you have to have the computational means to do that. It is very clear that CFS is not a single thing. It can include in varying degrees sympathetic nervous system involvement, change in the HPA axis, a metabolic component, etc.

Returning to the control strategy: we have an idea of the burden and the morbidity, we know who is involved, we still don't have a clinical marker, but we have things that can be used pharmacologically for getting into the path of physiology. What of course is left out of that is the fact that only half of people with CFS have even seen a doctor and 16-20 percent have been diagnosed and treated. You've got to get those people into the healthcare system. This is where public awareness comes in.

Once they're in, they must have doctors who can treat them and they must be eligible for treatment under their insurance policy. That is where provider education comes in. The information from the research goes to the provider education and public awareness efforts.

Committee Members Q&A

Dr. Jason: We've have heard that the CDC is having funding cutbacks. How will these affect your program? Has there been good epidemiology work on kids with CFS? There's been some controversy with the Wichita study using an empiric case definition vs. a usual way of doing that evaluation.

Dr. Reeves

On kids: CFS is primarily an illness of adults. It peaks in the 30-50 year-old group. It does occur in kids. It is perhaps more devastating at that time in one's life than it is for adults. Most of our research has centered on adults – that's where cases are and it's harder to deal with kids. Probably the most important group of kids is the teenagers. There's a real problem in dealing with people much younger than teenagers because they aren't acculturated yet and it's harder for them to express certain things. The provider registry is going to include all of the schools, all of the pediatricians, and the school nurses, so we are making an aggressive outreach to the adolescent population.

On case definition: It is a sticky issue. CFS is fatigue not relieved by rest that causes a substantial impairment in occupational, educational, recreational, or social activities. It is accompanied by four of eight symptoms. The problem is—and it's been a problem in all of the studies—I really don't know how *you* defined CFS in Chicago compared to how we defined

CFS in Wichita. We defined it the same way, but there is no standardized way to ask the questions about symptoms. What we have done more recently in our Wichita clinical study and in our Georgia studies was implement the recommendations of the International CFS Collaborative Group and use the SF-36 as a standardized instrument for measuring impairments. We used four of the eight scales. There is also the multi-dimensional fatigue inventory for measuring the dimensions of fatigue. We took two of the five scales. And then we devised our own instrument, which we published in *Psychometric Properties*, to measure the occurrence, frequency, and severity of the eight case-defining symptoms. Now our definition of CFS is that you meet at least one of the 36 SF criteria and at least one of the MFI criteria, that you have at least four symptoms, and that you meet a cutoff determined from the population. Now, what we call CFS is based on highly standardized instruments.

On funding: Our current budget is $4.3 million for FY 2007, which is at about the 1992 level. We're doing what we're doing now because of money we had under the payback. We cannot sustain the program at a pre-1992 level.

Dr. Klimas: If 85 percent of the patients are not diagnosed and half of them have not seen a doctor for their fatiguing illness, my question is about the other half. In my experience, medical care dollars spent prior to getting a diagnosis can be extremely high. I'm curious about what the healthcare cost is in the undiagnosed group.

Dr. Reeves: When we did the study that we've published, we were able to calculate the direct costs. We're just beginning analysis in the Georgia study and measuring much more accurately the direct and indirect costs, and we will certainly relate that to those who are seeing physicians and those who are not. It will probably take about half a year to work that up, but it will be specific, including metropolitan, urban, and rural economic impact. Our calculation was that it costs the United States $9 billion a year in lost earnings. What's important to me is the $20,000 lost to a patient's family. Diagnosed or not, the people in Wichita were out of work and on disability.

Mr. Newfield: With regard to the Georgia study, I hope quality of life issues will be looked at.

Dr. Reeves: Quality of life is part of the economics.

Mr. Newfield: I attended a conference for insurance companies and their attorneys where a doctor characterized CFS and FM as being either a somatoform disorder or merely psychological. If this gains any momentum, it could be disastrous to the community.

Dr. Reeves: CFS is a mind/body illness. You can't separate them. How can I deal with the perceptions? I do not have a diagnostic marker, but I can show you changes in cognitive functions that go to the frontal cortex and basal ganglia. I can show you reproducible changes. It needs to accumulate in the literature.

Mr. Newfield: My concern is that bundling these disorders would have a great effect on the population that suffers by giving the insurance companies a hook to say that this is a mental and nervous disorder to limit the period of disability pay. What is the CDC's position on bundling vs. bifurcating these conditions?

Dr. Reeves: We really don't have one right now. We're going to go directly off of the evidence. The insurance companies are interested in bottom line. If the bottom line is that treating and

appropriately diagnosing these conditions costs them less money, they're going to do it. Much of this involves the economics. We have not really done a lot with the HMOs and insurance companies yet. We're going to bring that in as part of the pilot registry, and we hope that we can change their approach based on knowledge.

Mr. Newfield: My concern is that by and large the insurance companies that handle the healthcare aspects are, generally speaking, different that the ones that handle the compensation and disability issues. Aetna and Cigna do both, but by and large they are going to have different agendas. The healthcare company is going to want less money paid out for the healthcare costs, while the companies that do disability don't want to recognize the disability condition, so they're not necessarily coming to the table with the same approach.

Dr. Joanne Cono

Over the past two years, the CDC has been undergoing a structural reorganization. The CFS research program at CDC was formerly within the National Center for Infectious Diseases in the Division of Viral and Rickettsial Diseases.

Under the reorganization, the three national centers that handled infectious disease entities—the National Immunization Program, the National Center for Infectious Diseases, and the National Center for HIV/AIDS, STD, and TB Prevention—were brought together under a Coordinating Center for Infectious Diseases and into four national centers:

The National Center for Immunization and Respiratory Diseases
The National Center for Zoonotic, Vector-Borne, and Enteric Diseases
The National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
The National Center for Preparedness, Detection, and Control of Infectious Diseases

With various programs being evaluated and realigned, it was a good juncture to look at the CFS program and where in the new structure the work could be supported. CDC embarked on a two-step review process of the program:

1. This winter, an internal planning group of CDC scientists from across the agency was convened for a two-day meeting to hear presentations from Dr. Reeves and other CFS experts. The group was then charged to understand the core activities and scientific accomplishments of the program to identify opportunities for intra- and extramural collaborations within CDC and with external partners. The group:

- Concluded that CFS program could build on its multidisciplinary strengths and that ongoing research of disease burden and economic analyses is important.
- Concluded that more could be done to explore psychiatric, neurological, and immunologic connections and to increase internal and external collaboration.
- Considered multiple placement options for the CFS program under the new CDC structure.

2. The CDC convened an external blue ribbon panel to review current intra- and extramural and external collaboration, to review the portfolio of future research agenda options, and to identify successful and problematic lines of research. The panel was not required to reach consensus when it chose the following areas of emphasis:

- Continuing the Georgia research activities.
- Continuing the refinement of the CFS case definition.
- Developing, applying, and evaluating new interventions.
- Increasing internal and external collaborations.
- Continuing multidisciplinary research.
- When considering multiple placement options, preserving the organizational strength of the CFS research program.

The group developed a final composite report, which is now with the CDC leadership for consideration about the future placement and research agenda of the program.

Committee Q&A

Dr. Jason: How will decreased funding for CDC impact the type of work that's going on at the CDC in this area?

Dr. Cono: I don't have any additional information other that what Dr. Reeves shared earlier. My understanding is that FY 2007 funding has been level and the future is an unknown.

Dr. Reeves: There are two issues. One is allocated funding and the other is payback funding, which went on the top of that. The allocated funding was approximately $4 million in 1998. Allocated funding was between $4 and $5 million in 1999. In 2000 it was a bit more; in 2002, allocated funding was approximately $6 million. Allocated funding has fallen since then to about the 1997 level.

Payback was finished in 2005. It came about when a problem occurred in using the monies allocated by Congress for CFS. CDC recognized the mistake and restored the CFS funding that was inappropriately accounted for. Total payback was $12.9 million over five years. During that time, the program was funded at $8 million a year, a level that cannot be sustained with allocated funding alone. The total CDC budget in 2005 was a little over $8 million. Our current allocation in 2007 is $4.3 million to the CFS program.

Dr. Oleske: The work that you said is still to be done in Georgia—is that going to be able to be funded at the $4 million level?

Dr. Reeves: We initiated the contracts for the studies that we are currently doing in the last year of payback funding, so that the first follow-up in Georgia, the provider registry, and the in-patient clinical study were paid for from payback funds. Those funds no longer exist. We can complete the studies that I listed, but there will be insubstantial money to do anything like that in the future.

Dr. Parekh: If the money stays the same, how much epidemiological work will be able to be done?

Dr. Reeves: New field work (surveying populations and following them up)—none. Analysis, interpretation, working up the data—lots. But the problem becomes that the momentum stops. At the bottom line, we have lots of analysis and interpretation—several years worth of that—but as far as doing anything with it after that…once process stops, you do not just start it again.

Dr. Oleske: It appears that for a variety of reasons, we're not going to see funding for the next several years for centers of care for large numbers of CFS patients. I'm concerned that while it was nice that we had this payback, from the point of support for CFS research, we're talking about the budget being cut in half. Those wonderful services we heard about in Albany are clearly not going to be available to those with CFS despite the fact that most of us would argue that those services are what our patients need. I probably don't have the right audience to answer the question, but it seems to me that however you slice it, we're going to see about a half cut in the budget for CFS for the United States in the foreseeable future, and I think that's drastic given the nature and extent of this disease.

Dr. Glaser: It would be interesting in the context of this discussion to find out the total number of CFS grants NIH funded over the last three years.

Dr. Oleske: CFSAC invited representatives from the professional medical associations to give presentations. None of them felt that it was a priority to send a representative to this panel. I'm finding out that we're still where we were 10 years ago with the professional physicians' groups not believing in CFS and our allies at CDC and NIH cutting back drastically on funding. CFS patients and their families are going to be left out in the cold.

Dr. Reeves: If I go to the Infectious Diseases Society of America or the Allergy Society, I get a standing room only audience. Those groups are particularly keen to have credible information on CFS, and we did not solicit the invitation.

Dr. Oleske: I may be misspeaking, and I apologize for that, but I still sense that there is a disinterest—at least among my peers that I see—for CFS.

Dr. Bateman: What is the future of provider education through the CDC?

Dr. Reeves: This is the last year of the provider education contract. We will be competing and advertising a new contract and we have the funding to pay for at least one year of it. It will be a similar type modified by what we're learned. It has a strong CME component and emphasizes getting information into medical school curricula via grand rounds that primarily target family practice, because that appears to be the group most interested. We are also targeting nurse practitioners and PAs. CDC leadership has bought into this enthusiastically. The Coordinating Center for Infectious Diseases is quite interested. There are crosses between other coordinating centers such as those involved in violence and chronic diseases as well as the cross-centers Public Health Genomics Working Group. We also have strong ties with the Health Marketing Group.

Mr. Newfield: Dr. Reeves, what will be the ultimate outcome of your body of work if you're compelled by budgetary constraints to stop the fieldwork?

Dr. Reeves: The fieldwork to do a population survey costs about $3 million. An in-hospital survey costs $1.5-$2 million. A provider registry costs about $2 million. Basically, we will analyze the data that we have in detail. We'll have data and one year's worth of follow-up, so we'll have some idea what the clinical course is for one year, as well as incident cases and economic impact over a year. We will have a pilot one-year provider registry and we will have one GCRC (general clinical research center) study. Early analysis should lead to the next study. Once you lose the cohort that you have picked up in a population survey and several years lapse, you cannot go back to it. There will be a lot of analysis and a lot of publication, but the ability to follow up on those will not exist.

Dr. Hartz: How much data do you have from the GCRC?

Dr. Reeves: The GCRC hasn't started yet, but those studies will be completed. It will be 120 patients—60 CFS, 60 control.

Update from CDC – The Public Awareness Campaign

Fred Fridinger, DrPH, CHES, Project Manager, *CDC CFS Public Awareness Campaign*
National Center for Health Marketing
Accompanying Document: *CDC's Chronic Fatigue Syndrome Public Awareness Campaign: Update to the CFS Advisory Committee*

The CFIDS Association is the main contractor for the awareness campaign along with Fleishman-Hillard, and they have done an exemplary job. I will update CFSAC on what has occurred since the media launch on November 3, 2006 and where we're going over the next year or two. This is a funded campaign through September 2009.

Major media outlets in broadcast, web, and print venues (NBC Nightly News, Fox News, CNN, *US News and World Report*) covered the campaign launch. We have seen an increase in media pickup since that launch. We released public service and print ads as well as ancillary materials such as the CFS toolkit for health professionals and a variety of other downloadable items. The toolkit has six fact sheets on evidence-based approaches for diagnosis and treatment and includes a sample brochure.

Highlights that demonstrate the broad exposure of the PSA through April 2007:

- Percentage of television plays between 6 a.m.-11:30 p.m. – 50 percent. This percentage during heavy viewing hours shows interest and high visibility for a PSA and speaks to its quality and the seriousness of CFS as a public health issue.

- Number of viewer impressions – 59 million.

- Number of projected radio listener impressions – 149 million.

- In April, print ads appeared in *Ladies Home Journal, People,* and *Better Homes & Gardens*. The combined readership of these magazines is 44 million. The number of "viewer impressions" (those who are exposed to the magazine in the same home or office as the subscriber) to date is 112 million.

- Online banner ads at the websites of the three magazines above have drawn 6.2 million viewer impressions. WebMD has drawn 475,000.

- The CDC campaign website (www.cdc.gov/cfs) shows a tremendous up kick immediately following the launch, rising from 11,617 downloads prior to November 2006 to 410,430 pages viewed following the press conference.

- The campaign puts a lot of resources into earned media – stories that cover CFS as opposed to paid advertisements. More than 1500 stories related to CFS and the campaign have appeared in print and broadcast media since the launch.

- More than 20 research and practice-oriented partnerships have been developed with professional organizations.

There is an evaluation being conducted by Porter Novelli using a survey tool called Health Styles that will measure public awareness about CFS. A similar tool called Doc Styles will measure awareness among medical professions, especially among CFS providers. The survey items were included last summer and will be included this summer as well to measure any increase in CFS awareness.

Future campaign activities

- The campaign will continue through the summer of 2009. We've just dedicated another $1.3 million for the campaign for a total of $2.3 million over the next several years.

- Future activities will take an integrated strategy approach with paid advertising, the traveling exhibit, earned media, continued use of the PSAs, increasing partnership activities, and collateral materials, particularly those that can be downloaded.

- CFIDS has again made purchases in *Better Homes & Garden* (August issue)*, People* (June 25 issue), and *Ladies Home Journal* (August issue). The purchases will total 17 full-page ads targeting women aged 35-64 who are most at risk. Banner ads will again appear on the magazine websites as well as on Web MD.

- The traveling exhibit will be located at Union Station next week and will go to Penn Station (Baltimore), and conferences of the American College of Physicians, the American Academy of Physicians Assistants, and the American Academy of Nurse Practitioners. We're looking at an opportunity to exhibit at the CDC's new Global Communication Center.

- We continue to look for earned media opportunities and are re-contacting editors to request that the PSAs be replayed.

- We're already coordinating a media response at CDC to coincide with the release of Dr. Reeves' research report.

- We will continue partnership development with the four CDC-approved organizations—the American Association of Physicians Assistants, family practitioners, nurse practitioners, and the Society for Women's Health Research.

Our center is uniquely situated from a federal agency perspective in that we have staff with skills and expertise to deal in various communication and marketing efforts. We have roughly four divisions within the National Center for Health Marketing:

- Division of Health Communication and Marketing Strategy
- Division of Partnerships and Strategic Alliances
- Division of E-Health
- Division of Creative Services

We are actively attempting to go trans-center from a communications marketing perspective. Every Center at CDC has a Director, and that person has an Associate Director for Communication. Under the reorganization, that Associate Director is now an employee of our

center. In essence, they are our representatives within the various Centers, Institutes, and Offices. We are trying to create those bridges so that public awareness campaigns are more integrated in program content and in terms of communication and marketing possibilities.

My own branch has just taken on a couple of new activities. Two of these are in public engagement and long-lead media. The public engagement is using innovative technologies to reach the public. These technologies include cell phones, YouTube, and other alternative ways to reach people beyond traditional communication technology.

Out long-lead media activities include a Health, Media, and Society Program that works with the University of Southern California's Hollywood and Media Society Program as well as with program writers and producers to promote public health issues. I don't recall anything being done on CFS, but this is a tremendous opportunity to explore how film, media, and TV can get CFS into the public eye.

Committee Q&A

Dr. Oleske: Since the message is helpful to a lot of Americans and it's politically neutral, it would be nice if some of the candidates in the debates would bring up the importance of supporting CFS.

Ms. Artman: The demographics tend to show that a large Hispanic community also has CFS. In looking at who this is being marketed to, I didn't notice anything that is Hispanic-oriented.

Kim McCleary (CFIDS Association of America): We did not have funding in the original budget to develop Spanish-language materials, and so we did not create outlets for reaching the Hispanic audience because we didn't have materials to deliver that were going to be consistent with the rest of the campaign.

Dr. Fridinger: We now have a group that provides multi-lingual services as well as some translation capacity in the Creative Services Division, so there is opportunity in the future to develop CFS materials.

Ms. Healy: Is there any way to know how many hits on the CDC CFS website went to the toolkit for providers to get a sense of who was looking at the materials? Is there a way to know how the toolkits were impacted by the public service campaign?

Dr. Fridinger: I think that the only way to obtain that information is to have an on-site survey, which I don't think was available.

Ms. McCleary: The way that CDC.gov is set up, there are no cookies or any way to identify where hits are coming from other than the referring URL. You can see the number of downloads of campaign materials in the statistics that Fred has provided that relate to the toolkit, but we don't have the capacity to discern who is downloading it.

Dr. Jason: It would be helpful to CFSAC as we try to get a handle on funding to get a breakdown of the different activities and the different funding amounts. A follow-up question—there's been a lot of discussion over the last year of what the name of this illness is, and I'm wondering whether you've given any consideration to the topic of the name—whether you use ME/CFS or some other name in terms of branding.

Dr. Fridinger: That's an interesting question from a communications standpoint. Given that I've just become more aware of this area in the past few months, it would seem to me that given the relatively short history of CFS in the public consciousness, the simpler, the easier to remember. There are two issues here. One is that once something is imprinted like CFS, it's very hard to change from a public perspective. The other thing is that the shorter terms and message slogans are, the easier they are to identify. If you want to make modifications, I think it's going to be difficult, although if you're going to do it, do it early on.

About the monetary—would it be something as simple as looking at these general activities and roughly how much is dedicated them?

Dr. Jason: Certainly that would be helpful. It would be helpful to know these different streams and how much it all adds up to—it could be more or less than we think.

Dr. Reeves: I just want to make a comment on the name. That is not a public health marketing issue; that is a scientific issue. I would like to point out that names are not just assigned willy nilly by HHS or CDC. There is not a published international case definition for CFS/ME. There was an internationally-accepted definition of CFS developed in 1994 that has more than a thousand references in the scientific literature. I am not aware of a published, internationally-used case definition for an illness called CFS/ME.

Dr. Klimas: We have to be careful—as we are a national advisory committee—what implications our work has on the international community. CFS/ME is a widely used name for this illness in other countries—the preferred name in many countries. By us strongly sticking behind the "CFS" without any slashes, we are more or less forcing this name in the international community. The Canadians did put together an international group to develop a clinical case definition and published that, and it is widely used and readily accessible.

My question to you is on a very different subject. Are there any copyright issues involved with downloading material from the public awareness website, including translating it into other languages? Is provider education in the public awareness budget or another budget?

Dr. Reeves: The provider piece is in the research budget because we developed it first, but they are two quite separate budgets. They are tightly coordinated, because in driving providers to the CDC or CFIDS website, we hope to get them into the CME website. But the provider education, since it's much more technical in nature, is a program activity.

Dr. Klimas: You are targeting physician extenders and family practitioners. Internal medicine doctors make up the vast majority of outpatient-based primary care. Why aren't we targeting them?

Dr. Reeves: We've got a limited amount of money that we can spend. We try to spend it where we get the biggest bang for buck. With the new contract coming out, we will have the same fiscal constraints as we have now. We seem to have a bigger bang for our buck from grand rounds and presentations than we do for other things, although these others are very successful. Ground rounds are targeting family practice, nurse practitioners, and PAs. We do the others, but we're aiming at these.

Dr. Klimas: I'd hope that you'd be able to widen that in some way, and if you can't, then maybe we can work with the Health Resources and Services Administration or someone else so that it can be done. This committee's charge is to come up with the bigger picture, and the

bigger picture is that they all need to be trained. We need to make this model accessible to the bigger group.

Ms. McCleary: Through the public awareness campaign, we have targeted medical media as well as lay media. As a result, there have been an increased number of CFS articles in the medical media—not the peer review literature, but the other publications that healthcare professionals read such as *American Medical News* and *OBGYN News* and a number of disciplines that are not being targeted by the provider education project specifically. Also, healthcare professionals read the *New York Times* and the *Chicago Tribune* and *People* magazine just like everybody else.

Dr. Hartz: When you say you target one specialty, how do you decide which one, and would it make sense to have training institutions self-select which group is most interested?

Dr. Reeves: It is difficult to get this into the curricula of medical schools. Ground rounds are great because they give access to people in training, they have both medical students and post-doctoral people, they have practicing physicians who are on the faculty, and other faculty. We have targeted those universities that have family practice because they have been particularly interested and there's a finite number. You can go multiple times.

We always try to get the bang for the buck, and OFFER is a good example. Utah put on a special conference of continuing medical education two months earlier where I was invited as a keynote speaker, and it coincided with the OFFER conference. Dr. Bateman set up grand rounds with both internal medicine and family practice. The Mayo Clinic is a group that may now be interested in grand rounds. That would be a very good group to hit even though they're not family practice. We won't turn down anything, but as far as our targeting and our resources, that is who we're aiming at.

Dr. Oleske brought up the humanism in medicine trend and pointed out that CFS can illustrate many of the issues around humanism. He suggested that CFSAC could take advantage of that trend to put forward the concept that CFS is a great model.

Dr. Hartz: If you get the word out to more education institutions and it creates so much demand that you can't cover them all, you can ask how many and what types of people will be in the audience and direct your resources to the highest priority.

Ms. McCleary: That is what we're doing. We actively solicit participation in grand round programs at a number of schools with family practice and other priority programs. But when we do get one booking, we try to expand it out to do programming at other schools and hospitals, including using technology for remote participation.

Dr. Fridinger: The materials are appropriate for most medical specialties; it's just a matter of getting it to them through their dissemination and training channels.

Dr. Papernik: Patients learn a lot about disease states from direct-to-consumer advertising and Oprah. Is there any pressure that you can exert to get Oprah to do a program on CFS?

Ms. McCleary: She did a segment on June 24, 1998, on hard-to-diagnose diseases and CFS was included in that. Fleishman-Hillard has a relationship with her company. *O* magazine included a lengthy article last summer and we were hoping that would translate into an appearance on the show, but so far I don't have any date to report.

Dr. John: In this groundswell that's taking place, we're going to produce what seems like a large number of new patients. This is a complex disease that cannot be taken care of easily by a primary care provider. Progressively, the more complex decisions in these cases must be made by physicians who focus on the disease. In a state like South Carolina, there are so few. In some states we don't have any named. We need to reach medical students in years one and two. It's OK to have grand rounds, but that's not a true curricular activity. Along with all your deliberations, I would recommend that we also concentrate on the ultimate development of a group of people to better take care of this complex group of patients.

Mr. Newfield: A North Carolina mother with a child with CFS recently approached me because she was unable to get care. The state Center for Health Statistics, Division of Public Health, wrote her back asking her to explain the acronyms "CFIDS" and "CFS", so they don't know the acronyms. Public awareness needs to be aimed also towards governmental agencies charged with public health.

[Dr. Oleske called a five minute break.]

Ex-Officio Updates

Dr. Marc Cavaille-Coll, FDA
Accompanying Document: *Food and Drug Administration Update*

The accompanying document includes background information provided at previous CFSAC meetings as well as contact information and other resources. Some highlights include:

- The Center for Drug Evaluation and Research is in the process of consolidating all of its divisions onto one campus. It has been enhancing our ability to consult with the other divisions that may have expertise that is useful in evaluating drugs, including CFS products. The collaboration is useful because of the multi-factorial aspect of CFS. Examples are the Chronic Cardial-Renal Division, which has helped with its expertise on exercise tolerance testing, the Pulmonary Division, which has assisted with oxygen consumption and respiratory issues, and the Neurology Division, which has been consulted on neuroendocrine issues.

- The Office of Special Health Issues is a source of information about development of products for diseases that are not very well understood or have unmet medical needs.

- The pre-IND (investigational new drug application) consultation program is intended to help investigators or companies that are starting in a new area such as CFS and need advice about what information they need to present for a successful IND. The program was created in the early period of development of drugs for AIDS, but has been expanding into many other areas with unmet medical needs.

- Our agency is not unique in that throughout FY 2007 we've had to deal with less funding than we expected to have, but the future looks brighter. A large part of our funding comes from the Prescription Drug User Fee Act, which has to be renewed every three years. We are currently negotiating with Congress and industry to do so. There is

going to be more money to fund initiatives dealing with drug safety issues, but not at expense of new drug development.

- Our activity in CFS has remained slow. An important step of drug discovery is having a mechanism of action or pathophysiological mechanism (CFS does not have these) so that companies can screen through thousands of molecules that could have a chance of benefiting a condition.

Committee Member Q&A

Dr. Papernik: Does FDA go through the same process for approving the new use of a drug that has already been approved for another illness?

Dr. Cavaille-Coll: Any company that has a lawfully marketed product for which it wants to develop a new indication is free to conduct a development program and clinical trials, then submit a supplementary new drug application or efficacy supplement with adequate, well-controlled trials, and we will review that. That's something that needs to be initiated by the companies if they want to do that.

Dr. Papernik: So they're subject to the same rigorous criteria as if they were bringing the drug before the FDA for the first time?

Dr. Cavaille-Coll: It's the same for every indication. The statutes say that there has to be substantial evidence of efficacy and safety as demonstrated by adequate, well-controlled trials. It's the same standard. There are other standards that have to do with manufacturing, potency purity, and toxicology which hopefully have been solved by then. A lot of the clinical pharmacology questions have already been answered, so the amount of information for an additional indication is expected to be smaller.

Dr. Papernik: Can you make any comment on the progress of ampligen?

Dr. Cavaille-Coll: I cannot comment on the status of a product that has not been approved. However, publicly traded companies do make such information public. Any information submitted to the Securities and Exchange Commission relating to the value of a company's stock must be correct.

Ms. Artman: You can actually call the manufacturer of ampligen, and they will give you all of the information.

Dr. Jason: If a product is running out in terms of its patent life and extending it to a new illness would also extend that patent life, pharmaceutical companies would have some economic advantage to develop evidence that the drug is effective with another illness. If there are not distinctions between a lot of these difficult-to-define illnesses, and if a particular product could be used to treat many of them, then pharmaceutical companies would have an implicit interest in not differentiating those conditions, thus extending the life of their drug patents. Is there any truth to what I'm suggesting?

Dr. Cavaille-Coll: If the patent exclusivity is expiring on a drug's use for one indication and the company applies for its use for another indication, the company will only get patent exclusivity for the new indication, not an extension on the indication for which it's already used.

There is an orphan drug program for products that fulfill an unmeet medical need. One of the criteria is that the prevalence of the condition has to be less than 200,000 in the United States. Once a product gets that indication, even if the prevalence is found to be larger, the product will still retain that designation for that indication. In CFS, we estimate that the prevalence is greater than 800,000. But as we do further CFS research that identifies a medically plausible subset whose prevalence is less than 200,000, a product that could treat that condition could be considered for orphan drug designation as long as there is no other drug to treat the condition. The orphan drug program allows a company to deduct some of the development expenses and get seven years of exclusivity for that indication.

Dr. Klimas: The driver in this field for sometime has been to understand CFS well enough for biologically subgrouping for targeted therapeutic interventions. There could be some economic incentives to a company to develop a drug for a subgroup under 200,000, and that might be a very good thing. The disturbing thing is the trend to try to lump a lot of groups together and to re-designate CFS as one of many of these smaller illnesses that might be lumped together as a target population for drugs that are reaching their exclusivity designation. Research is finally clarifying and giving us biological data that gives us a good strong sense of the biology of some of these subgroups. I would be disturbed to think that once we are finally getting there, we would jump back 20 years in policy logic and try to lump FM, TMJ, CFS and so on into one big homogenous group in order that a company would get a label that might give them exclusivity. Would the FDA be open or closed to the idea of lumping these conditions into some bigger umbrella name and saying that a drug is effective in treating it?

Dr. Cavaille-Coll: That's more of a scientific issue. How could you conduct a clinical study defining your enrollment criteria for these different populations and come up with evidence of safety and efficacy? I don't know of much precedent for successful development programs where companies have lumped such a wide variety of disease subsets and were able to statistically prove that they have a beneficial treatment effect in each one of them.

Dr. Hartz: Can you give us a general idea of the activity level of the filing of applications for medications for CFS treatment?

Dr. Cavaille-Coll: When we're dealing with an area where the public knows that there are only a few products being investigated, it will be easily discernible which products we're talking about. Activity for CFS is limited. Drug discovery is difficult because we don't have the science to select molecules that would be likely to succeed. With respect to drugs that were to have been investigated under INDs, I think I can stick to my previous estimate that it is still less than 20 for either primary or secondary indications. There has been a lot of research of lawfully marketed products, but these have not been conducted under INDs.

Dr. Deborah Willis-Fillinger, HRSA

HRSA agencies include:

- Bureau of Health Professions - supports health professionals' education and training.
- HIV/AIDS Bureau - has direct service dollars for HIV/AIDS care for patients as well as support of HIV systems that offer support services in the states. These include drug assistance and case management.
- Office of Rural Health Policy - includes funding for rural health system support.

- Maternal and Child Health Bureau - distributes block grants to the states for MCH services.
- Bureau of Primary Health Care - includes the Community and Migrant Health Center programs, public housing programs, and healthcare for the homeless.
- HRSA supports other health systems programs as well, including organ donation.

There isn't much that HRSA is doing specifically in the CFS area. HRSA doesn't traditionally care for disease-specific conditions, except for HIV/AIDS. Most of our dollars are for healthcare access and infrastructure to provide:

- Grants for medical, dental, and nursing education.
- The National Service Corps, which encourages providers to offer healthcare services in "health professional shortage areas."
- Clinic support for HIV/AIDS primary care.
- Grants for telemedicine and telehealth.
- Staff or support for professional clinical guideline work groups.
- Curriculum development support based on the different programs that we have across the agency.

Learning Collaboratives. Many of the programs, bureaus, and offices at HRSA are currently engaged in learning collaboratives. The community health centers are participating in health disparity collaboratives that focus on disease areas that are a priority for public health such as diabetes, cardiovascular disease, hypertension, cancer, and patient safety. The collaboratives are looking at processes that improve outcomes. They learn from each other nationally through best practices and redesign patient care to incorporate processes that have been found to result in the most effective outcomes for patients. We have multiple websites that the organizations can access to learn together. They have resulted in quite significant improvements for those programs that have been involved.

HIV/AIDS. HIV/AIDS is addressed specifically because the epidemic was affecting facilities supported by HRSA and those had to be equipped to handle the cases. HRSA has been involved in continuing HIV/AIDS education for providers to keep them up-to-date on changes in the epidemic and treatments. There are AIDS education training centers as well as The National Quality Center for HIV/AIDS Work. Performance measures, guidelines, and quality improvement coaching are continually available to providers on the front line.

New Activities at HRSA

- HRSA got reauthorization in January for its HIV/AIDS programs. HRSA will expand the number of communities that are funded for HIV. There is a huge ramp-up in sharing knowledge and ensuring that the providers and systems involved have access to as many of the resources as have been previously developed across the agency for HIV/AIDS.
- There is a trend in the bureaus and offices across the agency for increasing performance measurement and driving quality improvements. The agencies that we're involved with are being funded to make improvements slowly over time including systems to report performance data such as electronic health records.
- The National Service Corps has been incorporated into a new bureau that focuses on professional health service providers.

Committee Q&A

Dr. Oleske: CFS faces a similar problem as HIV/AIDS did with centers struggling to provide services with limited funding. Supporting CFS clinical trial groups and centers of excellence around the country is probably not going to be at the top of NIH's list. Yet the model that we had for HIV with clinical trial groups accomplished a lot. We prevented the perinatal transmission of the disease. Could HRSA be funded and empowered to support centers for CFS like you've done for AIDS? The only reason I say that is that model worked well for HIV and I think it would work well for CFS. Chronic fatigue is a disease in search of someone to support its clinical care programs. Would you ever conceive of HRSA being involved in supporting model programs that teach physicians at five to seven sites across the country?

Dr. Willis-Fillinger: I think that it could be done, but CFS may need a smaller approach than the 130 sites for AIDS. A start may be just a resource center, which has all kinds of training materials, and then a national clinicians consultation center. The AIDS education training center program is a $38 million program that has just been cut by $6 million.

Dr. Oleske: It would require a dedicated group like the CFS associations to really put that agenda forward, but to me that seems to be the only way that we start educating enough physicians to take care of and have the expertise to care for patients with CFS.

Dr. Klimas: It's not the CFIDS Association's responsibility, it is our responsibility as an advisory committee to ask HRSA to do exactly that. [Willis-Fillinger] just described the agency that could do what needs to be done—telemedicine, curriculum development, certification programs, and ways to make sure that the medical school curriculum provides this education, health disparities research, quality improvement measures, and electronic records.

Dr. Oleske: I've seen it done for HIV and I don't know why we couldn't do it for CFS.

Ms. Artman: Why couldn't the CFS provider packets be sent to the list of HRSA offices—here's free CME and here's information. Is this distribution something that you would see as feasible? I know that there's the cost of distribution, but there are electronic formats.

Dr. Willis-Fillinger: Electronic is easy, and there are clinicians' networks with listservs. It's obviously the hard copy that is more complicated.

Dr. Jason: I was taken by your statement that by starting small, there are some strategic things that could be done. You mentioned a couple of limited things that could occur. How does one start the process of dialog to get those things initiated?

Dr. Willis-Fillinger: The models that currently exist are easily accessible on the Internet [www.hrsa.gov and www.AIDSETC.org]. Take a look at those models and decide which pieces make the most sense, then as you think about your recommendations, that would give you something to work with.

Ms. Healy: Would it be possible for training grants targeting primary care providers and PAs to have a chronic disease model as focus area, with CFS listed as an option? There's a lot of power in to what goes into grant requirements.

Dr. Willis-Fillinger: The general approach is to not focus on one particular disease area on the health professions side. In terms of the health disparities collaboratives, the diseases that

have been chosen are the priority diseases in terms of health quality improvement in this country. I'm not sure how CFS would be incorporated.

Ms. Healy: I think that the grants generally say, "We're interested in projects that focus on x, y, and z." As we look at the paradigm shift from acute to chronic care, in would make sense to have HRSA say to medical schools and others who would be competing for those grants that it is interested in clinicians being prepared to treat chronic diseases. It becomes part of the culture that if this is important in getting funding, then projects are developed that become sustained in medical schools.

Dr. Willis-Fillinger: I'll take back your suggestion and try to look at it.

Dr. Laurence Desi, Sr., SSA

In response to concerns about adjudication, we developed CFS education. SSA has had a ruling in place for five years that provides adjudicators with the information needed to make a proper evaluation of a case. We also provide training for adjudicators that includes disability examiners and administrative law judges (ALJs). Federal reviewers were also included, but plans are in the works that may eliminate the position. We make the physicians who are a part of our program aware of the CDC website as well as the free CME credits through CFIDS. We do annual literature review updates to keep up with progress in the field that may be applicable to our adjudications.

Federal reviewers differ from ALJs. The reviewers were part of the previous Commissioner's Disability Services Improvement Plan. Part of the plan was to have cases go to a federal reviewing official, who would be an attorney with medical training to review the case in detail and pick up any errors of law that may affect the adjudication. The system was implemented in one region, but that is being put on hold.

Dr. Jason: The International Association of Chronic Fatigue Syndrome/ME has a new and improved website and I just want to mention that for folks who want credible information from a scientific organization. SSA has an interesting data source of people who are applying for disability for this condition. I'm wondering if you could update your previously published information for this group to see how many people are actually coming in and trying to get disability for CFS, how many are getting it approved, and whether there have been any changes over the last few years.

Dr. Desi: I will send a query to find out what information we can provide, although I won't have it before the committee adjourns tomorrow.

Dr. Oleske called on Dr. Hanna to inquire whether she had any comments as the *ex officio* representative of NIH.

Dr. Hanna: I will be rewriting the program announcement for CFS that I just put out because it's only good until November 1, which means October will be the last cycle. I invite you all to take a look at the program announcements—the RO3, the RO1, and the R21—and if you have any particular thoughts about what kinds of questions you might like to add to that, send then to me before July 1. They're on the NIH chronic fatigue website.

Committee Discussion

Mr. Newfield: The patient population has a real challenge in getting to CFSAC meetings and then feeling well enough to participate. How can we broaden access, whether that's through video or audio streaming? If you can assign some staff to addressing legal implications, let's work on identifying the solutions.

Dr. Parekh: We've talked about this issue before, and certainly it's something that we can continue to explore. There are probably some finance-related issues. To this point, when members of the public can't attend in person, they get updates from minutes of meetings and many advocacy organizations provide summaries. In terms of live video or audio, there are other HHS advisory committees that provide those. I welcome your suggestion.

Mr. Newfield: My understanding is that at least one of the advocacy organizations can arrange certain funding.

Dr. Parekh: Under federal government constraints, we can't work that way. Everything needs to be done competitively and transparently. We need to brainstorm other avenues.

Dr. Oleske: Going back to the AIDS model, one of the advantages of having a clinical trials group is that we had an advisory board that was actively supported by the center, and we paid for two advocates with HIV to come to the meetings. There was a mechanism in place for doing that—in fact we had that obligation. That's one of my concerns about not having designated centers that are supported, know about CFS, and can develop community advocacy groups.

Dr Jason: How do you choose *ex officio* members? Do they have to be within HHS or could they be outside of it, such as the VA or Defense Department? Have you considered bringing those folks in? How does the agenda get set up?

Dr. Parekh: The *ex officios* are designated by statute. Right now, of the five *ex officio* members, SSA is the only one who is not a part of HHS. CFSAC has discussed inviting other agencies. The committee has felt that it didn't want to include additional *ex officio* members, but rather invite others agencies and departments to come to speak. It is something that can be revisited.

The agenda for this meeting was developed through the work of the subcommittees. One of the tasks they were asked to do during the inter-meeting period was to decide what they want to focus on in the meeting. Subcommittee chairs got input from members. Ultimately, it is the chair as well as the executive secretary who have the responsibility to contact speakers.

Dr. Oleske: This is a very egalitarian panel. All that you have to do is participate in the conference calls and make your wishes known about the agenda.

Dr. Parekh: Each designated subcommittee chair could give a two-minute spiel today for those thinking of joining.

Dr. Oleske: The research subcommittee had two conference calls to try to come up with a research agenda. Our main recommendation is probably not going to be supported—six to eight centers of excellence similar to the model of HIV. The research subcommittee also came up with some concepts that we did think would be supported.

Dr. Glaser: I had a political issue to bring up. We were talking earlier today about clinicians and departments of medicine tending to ignore CFS. In science, I think the way things work is that nobody believes anything new until you have mechanisms, then suddenly it's credible. I suspect that part of the problem in dealing with the lack of respect from other clinicians to get involved in CFS (in addition to the money issue) is the fact that we don't have the faintest idea—even for acute onset CFS patients—what the etiology is. One question I would have for the NIH is, how much money is being spent related to etiology, focusing especially on EBV and HHV6, which have always been the two candidate viruses for CFS? It occurred to me that if we were lucky enough to establish some reasonable cause, the FDA becomes important for developing drugs that would be useful in dealing with those agents. I'd like to know roughly what the activity is at NIH and the CDC on etiology. The etiology issue has an impact on many of the issues that we've been discussing.

Dr. Jason: This is a foundational issue. I am still trying to get the big picture about where the money in this large system is going for different things. I don't know how as a committee we get access to that data in a way that we can summarize it so that we can see the big picture. Unless it is in front of us, it's difficult to make the kind of recommendations that are strategic and focused.

Dr. Hanna: Practically every year I've done a report on CFS for Congress, but those are only on the grants that are coded by program officers as CFS, so they by no means cover the things that you're interested in. All of NIH funded research is up on the NIH website listed in disease categories and dollar amounts. I can get you CFS-specific items so that you can see what each Institute spends on CFS. But all the NIH expenditures are on the NIH website.

Dr. Parekh: If there is interest by the committee to find published, transparent information about where dollars are being allocated to CFS, what's the best way?

Dr. Reeves: Put in an official request from the Executive Secretary to the Director of the CDC to provide you with a breakdown of the budget. I'm not sure how it's going to help the committee in any way.

Dr. Hanna: The only money that's counted at NIH is the amount that's spent on direct costs for investigator-initiated grants. Everything else gets picked up in the general budget. The CFS RFA awards—half of the funding for that came out of the budget of the Office of Research on Women's Health. Because we can't manage grants, we had to ask some of the Institutes on our trans-NIH committee if they would be willing to manage them for us. I can't say that we're going to have another RFA immediately because we'll have to see how this one turns out. This one ought to give us enough information to move forward in areas where we need to move.

Adjournment

Thursday, May 17, 2007

Call to Order/Opening Remarks/Roll Call

Dr. Oleske

Dr. Oleske called the meeting to order and noted that the prior day's presentations stimulated the panel to consider concepts that will help CFSAC make recommendations to improve the care of patients with CFS. He advised the committee that day two would be a focused work session with public comments presented in the afternoon. He said that the day's work would include subcommittee reports, the joining of a subcommittee by new members, and recommendations for creating new subcommittees if members see fit. Dr. Oleske informed the research subcommittee that because he serves as CFSAC chair, he would like to be replaced as chair of the research panel.

Dr. Parekh conducted the roll call and reminded the committee that it must edit the November minutes. All members were present except Kristine Healy, who returned to Chicago for a family function. Dr. Parekh declared that a quorum was present.

Dr. Oleske led the committee in providing edits and corrections of the November meeting minutes. After these were noted, a motion to approve the November minutes was seconded and unanimously passed.

Ms. Artman (Chair) reported for the Patient Care/Quality of Life Subcommittee

The subcommittee came up with several areas that need to be addressed:

- The name and diagnosis codes for CFS.
- Long-term disability and Employment Retirement Income Security Act issues.
- Social Security Disability Insurance complications and their negative impact on the waiting process.
- Request that the Centers for Medicare & Medicaid Services (CMS), Cigna, and Aetna appear before CFSAC, since the companies offer both medical and disability coverage. The discussion would cover what measures are used to mark improvement for disability purposes versus what is done for treatment. The subcommittee strongly feels the need to address third party payer issues at the next meeting so that CFSAC can determine what can be done to assist patients in using the system. There seems to be a conflict of interest. Medical insurance wants to go the cheapest route, while long-term disability wants patients to recover and go back to work.
- Return to work issues regarding people who can't work 40 hours a week.
- Medical care and treatment, including the lack of availability of doctors, finding doctors who understand CFS, and supplement issues. The subcommittee suggested that AHRQ (Agency for Healthcare Research and Quality) would be a good agency to consult.
- The social credibility of CFS. It's not just the physicians who need to be educated. There must also be community awareness that this is a real illness.

We agreed that third party payers is the first issue to tackle, because if we can understand third party payer issues and develop our questions, we will be able to help patients almost immediately see an improvement. We all understand that a doctor's appointment is nine minutes and I don't know anyone who can treat CFS in less than 15.

We were also interested in seeing if quality of life is being investigated in the Georgia studies (Dr. Reeves said that it is). We're interested in the outcome of how this illness is affecting

families and communities as well as individuals. We're gathering information to do a patient quality of life survey, although we didn't reach a conclusion about how that would be implemented.

Dr. Jason: I am interested in having someone from the VA as well. How do we decide who speaks before CFSAC?

Dr. Oleske: We sent out an email to CFSAC members soliciting suggestions about who they would like to address a meeting. One of the reasons that I picked Joseph John is that people wanted someone from the VA and he has experience with the VA. If you have a recommendation for a speaker, we'll try to get that person. They don't receive an honorarium, but they do get paid for travel.

Dr. Jason reopened the issue of including an *ex officio* member of the VA on the committee. Dr. Parekh replied that if CFSAC wants to add another *ex officio* member, it would need to be in form of a recommendation to HHS. Dr. Oleske noted that in the minutes from the last meeting, CFSAC clearly stated that the VA would be an important resource.

Dr. Klimas, who has also worked at the VA, suggested that Seth Eisen, a newly-appointed chief of research, would be someone to consider because he has done considerable work on Gulf War illness. She commended the VA on its provider education program and said that the committee might want to see who at VA would be most appropriate to address this topic. She noted that the VA did an outstanding train-the-trainer program for HIV, then put well-trained trainers in each VA facility. She suggested a committee session on provider education that examines available resources.

Dr. Hartz agreed that the VA has important skills and knowledge, but would have to be carefully integrated. With its strong concentration on post traumatic stress disorder (PTSD), the VA could shift CFSAC's focus. **Dr. Reeves** added that CFSAC was established to provide science-based advice and recommendations on CFS to the HHS Secretary. With the exception of SSA, the *ex officio* members are representing the various agencies of HHS on the Secretary's committee. Dr. Reeves did not think that adding other departments of the federal government to CFSAC would be consistent with the charter. Adding Gulf War illness, no matter how much it is similar to CFS, is not what CFSAC is doing, said Dr. Reeves. He expressed worry that rather than focusing on key issues that can be resolved, CFSAC would bite off a huge number of issues that would dilute firm recommendations in specific areas. Having VA speak on provider education and other topics relevant to the committee is what would be helpful.

Dr. Klimas commented that 30 percent of adults are veterans and a vast number of adults in the country receive their care at the VA. She pointed out that most of her and Dr. John's clinical patients have CFS, not Gulf War illness. Dr. Reeves replied that CFSAC's purpose is to advise HHS, not VA. He said that although everything that Dr. Klimas cited is true, that does not mean that a VA representative has to be an *ex officio* member.

Dr. Hanna said that regardless of how the committee handles the VA's status, CFSAC could learn a great deal from the agency. This includes not only what it does for education and medical records, but the way it pays for healthcare and what conditions it allows and disallow. The committee has a lot to learn from the whole psychiatric aspect of people not getting treatment when they're categorized as a long-term psychiatric disability. She advised that CFSAC learn everything that it can learn from the people who can teach whether they're in

HHS or not. She cited the Department of Education and its expertise with educational materials as another example of useful knowledge outside of HHS.

Ms. Artman agreed that the VA is worth looking into, but said that her subcommittee wants AHRQ as an *ex officio* member.

Dr. Jason noted that he made a motion that CFSAC recommends that a person representing the VA join the committee as an *ex officio* officer. He offered a friendly amendment to broaden the motion to include AHRQ. The motion was seconded.

Mr. Newfield asked for more discussion before taking a vote. **Dr. Oleske** noted that CFSAC was in the middle of committee reports, and official recommendations are usually made at the end of the meeting. He said that CFSAC could take the vote up later that day or have the discussion. **Dr. Parekh** recommended that CFSAC delay discussion of committee recommendations until the subcommittees complete their reports. Dr. Jason agreed that his motion could be tabled.

Mr. Newfield asked Dr. Reeves what type of quality of life/economic issues are being included in the Georgia studies. **Dr. Reeves** said that he would provide information on specific questions, hypotheses, and what is collected at the next CFSAC meeting. **Dr. Hanna** noted that NIH agency-wide planning groups have been meeting to develop a comprehensive quality of life measure. **Dr. Parekh** said that he would work with Dr. Reeves to gather the information about the Georgia study by the next quality of life subcommittee conference call. Dr. Reeves said that he would not be able to report on results, but could discuss the strategy of those questions, specific hypotheses, and what CDC hopes to get out of the data. **Dr. Oleske** said that he would provide the subcommittee with the quality of life tools that he has used for monitoring children and adolescents.

Ms. Artman asked Dr. Hanna to clarify the nature of the quality of life group at NIH. Dr. Hanna explained that it has been going on for a number of years and probably also includes HRSA and FDA. The group is preparing the quality of life measures so that they will be consistent over clinical trials. Dr. Hanna said that she will find out how ready the group is to make a presentation.

Mr. Newfield noted that the subcommittee has drafted a letter that it was hoping that HHS would send to third party providers in order to collect data on the incidents and prevalence of CFS, the kind of drugs covered, and medical costs associated with providing care for CFS patients. He asked for guidance on how to proceed. **Dr. Parekh** explained that the next step is to seek agreement of the full committee that the subcommittee should continue to develop the data collection request. That wouldn't necessarily be a recommendation to the Secretary.

Dr. Reeves emphasized that the issues discussed in the letter are central to all of the subcommittee and CFSAC as a whole. The issues pertain not only to quality of life, but education of providers and healthcare. He added that it would not be meant to be an inquisition of the third party providers, but an opportunity to gather information. Mr. Newfield agreed that the issue extends to the whole committee and although CFSAC may be unhappy with the results of the information, the session would not be an inquisition.

Dr. Jason inquired whether the committee should attempt to get information on touchier issues such as how many individuals companies process for CFS, how many are being reviewed, and how many have had their cases denied or terminated in some way. Mr. Newfield replied that

from his experience in advocating for disability claims, those areas would become confrontational much sooner than the issue of healthcare coverage costs. He said that the easier angle to talk about, in a global setting, is the treatment options, what companies will and won't pay for, and the incidence and prevalence of patients. He identified Cigna and Aetna as the two carriers that cover both disability and medical treatment and noted that there is interplay between long-term disability claims and healthcare costs.

Dr. Klimas inquired about a past CFSAC meeting at which the SSA reported on claims, approvals, denials and regional patterns. **Ms. Artman** said that Dr. Desi presented the report showing that not all people filing for disability list CFS as their primary symptom. When the claim goes into the system, the first disability listed is what is evaluated. Dr. Klimas asserted that the bigger issue is claims disapproval patterns that vary judge-by-judge and region-by-region.

Dr. Desi said that one of the changes made by SSA was putting in a specific impairment code for CFS so that SSA can specifically identify those people who receive benefits based on CFS rather than grouping them under miscellaneous. This would not capture people who claim CFS as their primary disabling condition, but are granted benefits under a different co-morbid condition. SSA stresses getting to the proper adjudication as quickly as possible. Whatever condition will produce the quickest decision is the one that SSA will to go with. But data collected since the CFS impairment code went into effect would be most accurate.

Ms. McCleary said that a nonbinding CFS impairment code was created in 1995, but is still somewhat voluntary as far as how the paperwork is processed. She agreed that SSA data would not tell the whole story.

Dr. Oleske requested that Mr. Newfield draft a data-gathering letter for third party providers. Mr. Newfield suggested that he will distribute the letter that he had already drafted for CFSAC members to read and take up later.

Dr. Bateman reported for the Education Subcommittee

The subcommittee conducted two conference calls on February 26 and March 28. The committee consists of Dr. Healy, Dr. Bateman, Dr. Papernik, Dr. Willis-Fillinger, Dr. Hanna and Dr. Reeves.

The subcommittee's purpose statement: The Education subcommittee wishes to promote the integration of education about chronic fatigue syndrome into the healthcare delivery system so that the care of people affected by CFS will be improved. The Education Subcommittee will focus on opportunities through HHS to enhance the education of health care providers and others within the healthcare workforce about chronic fatigue syndrome. The education of individual clinicians as well as the public and private entities involved in healthcare delivery is of interest to the committee. Topics such as the identification, development, and dissemination of CFS education resources and evidence-based best practices will be deliberated and motions brought to the CFS Advisory Committee at its biannual meetings in order to facilitate the development of education-related recommendations to the Secretary of HHS.

We discussed speakers we would like to hear and decided that we would like to ask Dr. Reeves or a representative from the CDC to report about what was learned about patient management from your studies.

During our discussions we realized that we hit up against a wall again and again because we don't know what to educate people about. We don't have treatment recommendations. We can teach people about diagnosis, but we don't have a lot of information about management. We also wondered about what resources were available from the VA.

Education Subcommittee Draft Recommendations (which Dr. Bateman presented as a list of ideas rather than comprehensive or complete items) in order of priority:

1 – A letter sent from the Surgeon General (SG) to state health departments; health professional education programs; and national organizations for physicians, PAs, and other allied health professional groups informing them about the CDC and NIH CFS resources including the CDC toolkit and CME course. The subcommittee created a list of potential recipient organizations and asked CDC if it has information about the impact that the toolkit has had so far on educating healthcare providers. The subcommittee noted that the letter could be disseminated online using resources that are easy and inexpensive.

Dr. Parekh explained that such a letter would probably have to go through a formal process of being put in a recommendation to the HHS Secretary, who would in turn direct the Surgeon General. **Dr. Reeves** said that CFSAC is of tremendous benefit for the CDC research program beyond the group's formal recommendations. He said that a large number of modifications have been made to the program based on committee discussions, including modifications to the registry and the formulation of the population surveillance. He added that committee discussions also have a tremendous impact on NIH and FDA as well.

Dr. Bateman clarified that the subcommittee did not draft a letter, but recommended that the Surgeon General draft a letter with resources provided by HHS, CDC, and NIH. **Dr. Oleske** suggested that something be fleshed out by CFSAC, and committee members debated the merits of whether or not to draft the letter. **Dr. Parekh** noted the feeling of the subcommittee that it might be better to give the SG's office more flexibility in how to write the letter instead of drafting it and seeming to be more aggressive. **Dr. Jason** suggested a compromise in which the Secretary would direct the SG to write a letter, then the SG could have the option of drafting the letter or enlisting CFSAC's assistance. **Dr. Bateman** noted that the recommendation itself would probably contain most of the content of the letter. **Mr. Newfield** noted for the record his strong feeling that state agencies charged with the responsibility of caring for the public at large should be educated.

Dr. Reeves commented that a letter from the SG will be read, but might not have a strong impact. There is an annual meeting of the Council of State and Territorial Epidemiologists, and the CDC could schedule a presentation at that meeting to talk about CFS and promote everything that the committee wants to promote. He said that such a presentation would have much more of an impact than a letter from the SG.

Dr. Bateman emphasized that the scope for the letter distribution is broad to include state health departments, health professional education programs, and national organizations for physicians, PAs, nurses, and other allied health professionals. These are three large areas, and some may be more attentive to a letter from the SG than others. **Dr. Reeves** noted that CDC is going to the annual meetings of several of those national organizations and presenting them with these toolkits.

Dr. Bateman explained that the subcommittee formed its recommendation with the recognition that these one-on-one activities are ongoing, but the panel had a sense of urgency that it

wanted to target a large number of people, give them access to the information, and continue the one-to-one in the background.

2 – An investigation of how to put new technology to use for inexpensive outreaches. CFSAC should do more brainstorming about how to use existing systems such as HRSA's regular emails to public health services.

3 – Investigation of new methods of provider outreach and education, primarily to the physician community. The subcommittee discussed HRSA's HIV model and how it uses a supportive educational and clinical network. The panel asked Dr. Willis-Fillinger to prepare a description of AIDS training and education centers and present it to the group.

4 – Enhancing and enriching the CDC program to train physicians, expanding it from a one-hour CME program to a three-hour training program that includes more information about treatment. The recommendation would be to empower/fund CDC to develop a more expanded provider education program and recruit more people to give the train-the-trainer presentations.

5 – Explore HHS resources to provide incentives for healthcare providers to train in the area of CFS.

Dr. Willis-Fillinger clarified that number three was not meant to be limited to the physician community or focus on HRSA exclusively.

Dr. Oleske (Chair) reported for the Research Subcommittee

In August 2004, there was a recommendation to form a network of five sites to provide education, care, and research for CFS. Page 40 of the November 2006 minutes includes a further discussion of that same concept, verifying that it is an important one that would advance research in CFS by having groups of investigators supported.

We also talked about the training grants available and how we can encourage colleagues in CFS to apply more aggressively for funding that is already out there.

We talked about the problem with case definition and the need to make sure that we have some coordination between CDC and NIH for the definition.

We discussed how to get pharmaceutical support for drug trials of medications already in use that are being used to treat CFS off label or any drugs that are appropriate to do a clinical trial with. The two areas of discussion that we would like to present to the committee are:

- The network concept of expert centers in which education, teaching, and research are going on. Each one of those centers would serve as many others as they can reach out to.

- Whether we should send the letter to as many researchers and clinical care providers as we can in the country to solicit responses to a number of questions on off-label medications, compile a list, and use it to influence drug companies to do trials of drugs that they already manufacture.

Dr. Hartz said that centers are important but can be limiting because you can have clinicians who aren't involved in education and research, you can have researchers that don't teach, etc.

Patients at these concentration points aren't necessarily the same as the patients at other places. Also, if you want to do more controls, you have to have a more diffuse source of patients and clinicians so that you can compare how different patients respond to different kinds of treatments.

On the second recommendation, to convince a drug company to do something, there should be some observational studies showing that there is preliminary evidence that a particular treatment might be advantageous for particular types of patients. He said that the groundwork has not been laid yet.

Dr. Bateman described a collaboration being developed in Utah in which a small and growing group of clinicians are collaborating with researchers at the university who don't have patients but are relying on clinicians' patients and referrals. The other arm is OFFER, which has been doggedly pursuing education. The group is growing its research, clinical, and educational capacities together, and Dr. Bateman said that the collaboration is generating the momentum. She said that the facilities can't afford to have centers in rural areas, but they do draw from rural locations through educational outreach. The university is a multi-state center with a growing research department that is gaining in stature. It's an example of how alliances can build a good combination of clinical, research, and education, she concluded.

Dr. Hartz agreed that alliances are beneficial and could be essential, but there are many different ways of achieving those things. He suggested that the recommendation be limited to stating what should be done, not limiting how it should be done. The proposal specifies in advance not only goals, but methodology, he said.

Dr. Oleske encouraged comments on the drug clinical trials recommendation, noting that there is no need to wait for an etiology before starting to take care of patients. The AIDS clinical trial groups were set up before the virus was isolated.

Dr. Hartz said that his impression is that clinicians managing CFS patients do not rely for treatment on one magic bullet. They have complex therapies that are not simple to present to a drug company. A better understanding is needed of the types of treatments that are effective, and he suggested that clinicians are not at the point of knowing exactly what they're doing and how effective it may be. **Dr. Oleske** inquired whether surveying clinicians about their off-label medications would be useful. **Dr. Hartz** agreed that it would be useful to substantiate what they're doing and what the outcomes are. But clinical trials are expensive and labor-intensive, and he concluded that the field is not there yet.

Dr. Klimas disagreed, noting that treatment guidelines are being written even though the only treatments that completed the clinical trials process are CBT and exercise. Clinicians are all using off label drugs for which patients are being denied insurance coverage. She said that the field is 20 years along and should have a clinical trials group to hammer out the priorities and scientific approach. **Dr. Hartz** clarified that he supports conducting clinical trials that involve collecting the evidence and doing a systematic analysis of that evidence but the field has not advanced to the randomized clinical trial stage.

Dr. Reeves interjected his view that it is not the function of CFSAC, which advices the HHS Secretary, to solicit and set up a research network. **Dr. Oleske** noted that CFSAC already made a recommendation at its last meeting to establish a CFS clinical trials network patterned after HIV clinical trials. **Dr. Parekh** clarified that it was not a recommendation, but an idea that was launched. Dr. Oleske said that the CFSAC can recommend that clinical trials network is

an appropriate response, noting that the details are not the committee's purview. Dr. Reeves suggested that the HHS Secretary may take CFSAC recommendations more seriously if they are highly focused, saying that while a clinical trials network is vital, making a recommendation on it dilutes from what CFSAC is doing.

Dr. Klimas described the debate as encompassing two things at once: the recommendation for the Secretary to overcome any barrier that would prevent establishment of clinical research centers, and the discussion of a survey instrument. It may not be reasonable for this committee to be surveying physicians, she said. Putting on her private sector hat, she volunteered to make sure that a survey goes out to the providers who are members of the International Association for Chronic Fatigue Syndrome (IACFS/ME). **Dr. Parekh** suggested that the idea would need more discussion and a committee consensus before it is launched.

The discussion shifted to the remaining agenda, with Dr. Parekh reading from the CFSAC charter the purpose of subcommittees. He suggested that the committee could officially address how many and which subcommittees are to continue and determine the membership of each. Then, before making specific recommendations, CFSAC could discuss what it wants to focus on, its goals, and how much it wants to accomplish.

Dr. Hanna noted that over and over again the important thing that comes up is research centers. The major obstacle to those is money. **Dr. Willis-Fillinger** suggested that in its discussion of priorities, CFSAC consider how best to use its two-day, twice-a-year meetings and whether there are activities that should take place between meetings to make them as productive as possible.

[Dr. Oleske called a 15-minute break.]

Formation of CFSAC Subcommittees

Dr. Oleske led the group in deciding on subcommittees and membership. A motion was made, seconded, and unanimously approved to continue with the Patient Care/Quality of Life, Education, and Research Subcommittees.

Dr. Oleske requested that someone replace him as chair of the research subcommittee and withdrew his membership on any subcommittee, noting that as CFSAC chair, he attends the conference calls of all three. CFSAC established that the **Research Subcommittee** membership now includes Drs. Glaser, Hartz, and Jason and *ex officio* members Drs. Hanna and Reeves and Dr. Jason as chair.

Dr. Parekh described the logistics of subcommittee conference calls, noting that it is the designated federal official's responsibility to schedule the calls, ensure that lines are set up, inform subcommittee members, and sit in on the call. Dr. Parekh said that over the past couple of months either he or the CFSAC chair emailed subcommittee members asking for the best dates. Dr. Parekh arranged for a phone line and call-in number for about an hour and a half.

The **Education Subcommittee** membership was established as Drs. Bateman, Klimas, and Papernik; Ms. Healy; *ex officio* members Drs. Hanna, Reeves and Willis-Fillinger; and Ms. Healy as chair.

The **Quality of Life Subcommittee** membership was established as Ms. Artman, Mr. Newfield, and Dr. Snell (who had excused himself due to illness); *ex officio* member Dr. Desi and Ms. Artman as chair.

Dr. Oleske asked the subcommittees to segregate into different rooms for a working lunch during which they could get acquainted with new members.

Open Discussion of VA/AHRQ Recommendation

Dr. Oleske opened the floor for discussion of Dr. Jason's motion to create an *ex officio* position for a VA representative and said that he is in favor of the motion. Dr. Oleske noted that although CFSAC is a committee of the HHS Secretary, SSA is an *ex officio* member that is not within HHS. **Dr. Klimas** said that *ex officio* members can serve multiple purposes, noting that Dr. Hanna, for example, has served as a tremendous resource in the fields of research, education, and policy. The VA could provide more than one area of expertise to CFSAC—patient care issues, research programs, and provider education.

Dr. Cavaille-Coll said that in the past, the VA has been asked to send someone with expertise to address specific issues and questions rather than serve on the committee. He suggested that it might be helpful to CFSAC to determine specifically what assistance it needs from VA and let the agency pick the person best qualified to address that specific topic. The VA representative wouldn't have to be an *ex officio* member to lend expertise to subcommittee conference calls or CFSAC meetings. **Dr. Bateman** said that it would make more sense to have a VA *ex officio* member than one from AHRQ, and suggested separating Dr. Jason's motion to vote separately on the agencies' status.

Dr. Klimas moved that CFSAC should table Dr. Jason's motion and invite a VA representative to the next meeting to explore what the agency could offer. The focus would be on provider education and CFS/Gulf War syndrome. CFSAC tabled the VA motion.

Dr. Oleske explained AHRQ's mission as monitoring the quality of guidelines to assure that they are evidence-based. The agency both reviews and commissions guidelines for areas where there have not been guidelines. AHRQ commissioned the first AIDS guidelines in 1986, for example, and also established smoking and pregnancy guidelines. **Ms. Artman** added that every AHRQ publication addresses quality of life within certain issues, and that is one of the reasons that the subcommittee wanted that group to get involved.

CFSAC voted to table the motion on AHRQ's possible addition as an *ex officio* member and invite a representative to the next committee meeting. **Dr. Reeves** reminded the committee that it already intended on focusing its next meeting on third party providers and that having two agency representatives in addition to that may crowd the agenda.

Open Discussion of Committee Recommendations

Dr. Klimas read a motion based on the Research Subcommittee's report:

I move that the CFSAC recommend that the Secretary establish five regional clinical and research centers—centers which would provide care to a critically underserved population, educate providers, and serve to develop research networks. The Advisory Committee understands that fiscal exigencies have to date prevented formation of these previously-

recommended centers, but it is our hope that the Secretary will use the full weight of his office to effectively fund this program.

The motion was seconded and opened for discussion:

Dr. Hartz recommended that the motion be sent back to the Research Subcommittee to discuss more specific goals and how to address them. **Dr. Glaser** supported the motion and cited the establishment of the NIH's Centers for Mind/Body Medicine as a successful mechanism model. **Dr. Jason** also supported the motion and said that it provides an interesting vehicle for galvanizing work on all three subcommittees. Research in these types of centers would provide infrastructure support for a younger generation of researchers; contribute to the education mission by interacting with communities, states, and other organizations; and influence work on quality of life.

Dr. Papernik supported the motion, commenting that it tries to do what CFSAC is supposed to do, and that is to give guidance so that information can be disseminated and the whole process of CFS and its future is promoted. **Dr. Reeves** said that the idea is tremendous and would greatly further research, but the committee has already made this recommendation and HHS does not have the money to set up centers. The appropriate way to pursue that is for organizations like the IACFS/ME to lobby the legislative branch.

Dr. Hartz inquired about the definition of "research networks"—do they include only centers?
Dr. Klimas responded that it is the goal of the centers to develop research networks that include both clinical and research centers that collaborate regionally and nationally. In reference to Dr. Reeves' comment, she said that it is a powerful tool when CFSAC recommends and even re-recommends an item. It empowers other groups to go to Congress and ask for line item budget support. The committee has not asked for any funding to date. The Secretary needs to hear CFSAC say that $50 million from the U.S. budget is needed to serve a population of Americans where 90 percent of patients are undiagnosed and 50 percent of doctors do not even know that the diagnosis exists.

Dr. Glaser suggested that the recommendation be much more explicit in discussing research, including basic and clinical. He emphasized that even if funding is not available and the recommendation is rejected, it is important that CFSAC send out the message that centers are an important way to go.
Dr. Jason agreed that good research will ultimately lead to best practices and good clinical care. He asked for clarification on the parameters of CFSAC work outside making recommendations to the HHS Secretary, noting that the discussion has included influencing Congress through advocacy groups. **Dr. Parekh** repeated the chartered purpose of CFSAC is to provide advice and recommendations to the HHS Secretary. These could involve the Secretary directing an organization within HHS or asking an external organization to do something. These recommendations go to the Assistant Secretary for Health and then directly to the Secretary's office.

Dr. Hartz said that his concern about the recommendation is that centers will be developed to the exclusion of other approaches. The centers in which patients are treated may not be located where there is research expertise, and the types of patients in a center may not be representative of all CFS patients. Recommending the creation of centers is not only setting goals, but limiting the methods of achieving those goals. **Dr. Klimas** proposed research/clinical centers because they are less expensive than setting up the two types separately. It would be wrong, however, to use only the center population—diversity is

important and research applications would be weighted accordingly. **Dr. Hanna** noted that if NIH were to be designated to set up the centers, its criteria for awarding grants would strictly require population diversity.

Ms. Artman said that without a center program, the CFS field will not just stagnate, it will decay and patients will not have a place to go for treatment. Centers would fill a desperate need. Private facilities are expensive.
Dr. Jason said that networking by the centers in the community of other scholars and would bring a critical mass of the best minds into the CFS field that are not there right now.
Dr. Willis-Fillinger suggested that the recommendation include a better description of what components the proposed network should have. **Dr. Klimas** said that if the recommendation was held until the next committee meeting, she could talk with committee members about specific language. **Dr. Hanna** suggested looking at RFAs for various kinds of centers, which will reveal that there are a variety of programs already established that have all of the elements being discussed. NIH already has mechanisms for everything being discussed. **Dr. Glaser** noted that outreach by the centers to community and other researchers would be important.

[Dr. Oleske called a break for lunch.]

Public Comments

Mary Schweitzer, PhD, *CFS Advocate*

Dr. Schweitzer said that she speaks for many people, including those overseas, who contact her via the Internet because they know that she lives close enough to attend CFSAC meetings. What the U.S. CDC and NIH say is heard throughout the world, she said, and concern has been expressed over a sentence that appears in the materials of the CDC public awareness campaign about CFS: **"There are no tests and there are no treatments."**

That sentence is very costly to patients:

- It makes it hard to get disability and medical coverage for procedures and testing. The default option is psychiatry. The first requirement for a somatic illness is that there is no evidence of physical causation. The quoted sentence turns that around to say that if there is no proof of a physical causation, then it is a somatic disease. As long the CDC supports this sentence, the people in Great Britain who are being sent into mental hospitals against their will by people who assert that CFS is a completely psychosomatic disorder are left with no support.

- While CFS is not formalized in the United States into neurostenia, it is usually stated as a problem handling stress, which still classifies CFS as a personal problem, almost a character flaw.

- Researchers are denied information that would help push the knowledge, physicians don't know about what they could use, and patients don't get treated.

As an illustration of the third point, Dr. Schweitzer noted that CFS patients tend to have abnormally low levels of cortisol. A physician making such a finding would suspect Addison's

disease, but once CFS comes into the discussion, the finding gets put into a much more far reaching model that hasn't been formalized. What is perhaps biological evidence that could be useful to some patients is deleted from the evidence base.
Dr. Schweitzer said that she was tested for a variety of conditions, treated for each one, and has gotten much better as a result. The tests included: Romberg's, NMH POTS, Hashimoto's, thyroiditis, hyperthyroidism, oxygen reuptake during a treadmill test, low natural killer cell function, chronically reactivated Epstein Barr virus, and active HHV6a. Dr. Schweitzer tested positive for all of these conditions. Her doctor took what was known about each and treated them individually.

Marly Silverman, Founder, *PANDORA (Patient Alliance for Neuroedocrineimmune Disorders Organization for Research and Advocacy)*

Ms. Silverman commended the advocacy work of Ms. Artman, whose contributions to PANDORA Ms. Silverman credited with shaping its growth and success and reenergizing the advocacy community. Ms. Silverman and Artman worked with the IACFS/ME board to bring the organization's 8th annual IACFS/ME conference to Florida. Ms. Silverman also explained The Empty Chair Project; each time she attends a CFSAC meeting and sees an empty chair in the public seating, she will place the picture of a CFS patient so that CFSAC members have an idea of how many people want to attend but are too ill to do so.

Ms. Silverman said that one of the things that is dear to her heart is a center of excellence or an institute. PANDORA has actually worked with Florida Sens. Mel Martinez (R) and Bill Nelson (D) to file an appropriations request for the Florida Neuroendocrineimmune Institute. The request for the past three years has been $1.5 million. Information about the request was sent in a February 10 letter to HHS Secretary Leavitt. Ms. Silverman also expressed the hope that the OPASI Roadmap Initiative will offer opportunities for the development of CFS research. It is up to researchers and physicians to learn how the initiative will work, she said, and she intends to meet with OPASI Director Krensky to give her input.

Ms. Silverman also called for:

- Increased awareness education for the Department of Health in Florida, which does not recognize CFS.
- A speaking invitation from CFSAC to a member of the Research Center at the University of Florida in Gainesville, where CFS is recognized.
- An FDA approved drug for CFS.

Eileen Holderman, *CFIDS Association of America*

Ms. Holderman informed the committee that due to her advocacy/lobbying schedule on Capitol Hill that week and attendance at the previous day's CFSAC session, she was physically unable to prepare separate testimony. She instead read from an article she wrote about her previous lobbying efforts. She expressed the hope that the information will:

- Inspire advocates to continue in their endeavors to affect public policy to benefit the CFIDS community.
- Establish a benchmark to gauge how well the federal government has responded to advocates' past requests for action.

The article described the 2005 CFIDS Lobby Day, which coincided with International CFIDS/Fibromyalgia Awareness Day. She explained in the article that her deadline was in the spring, but her illness kept her from completing her piece until the fall. One purpose of Lobby Day, she said, was to convey the seriousness of the disease and lack of widely applicable standard treatment protocols. Advocates requested from Congress:

- A letter to NIH Director Elias Zerhouni asking for an RFA.
- Creation of an Office on Trans-NIH Initiatives.
- Sign on to a letter to the HHS Secretary asking him to implement 11 CFSAC recommendations.
- Contact of relevant Congressional subcommittee members to increase CDC funding to $8.9 million.

Barbara Soliday, Miami CFIDS Support Group, *on behalf of her daughter Kristen, who has CFS*

In 1998, Kristen was a junior in college when she got a bad case of the flu and never recovered. She had expected to have her PhD in physics by now, nine years later. Kristin used to sit at the dining room table late into the night working on calculus for the sheer joy of it. She can't do that anymore. The American scientific community has lost a fine physicist and mathematician to the brain fog of CFS.

Kristin is getting state-of-the-art medical treatment from Dr. Klimas. But Ms. Soliday said that what frightens her most is the thought that Dr. Klimas will be hit by a car or fall off one of her horses. There's no backup doctor in Miami, Dade County, or the state of Florida for Kristin, or for hundreds of other patients that Dr. Klimas sees or the hundreds of others on her waiting list.

Our most urgent need right now, said Ms. Soliday is to take the knowledge that doctors already have and transfer it into the brains of people in medical school, doctors already in the community such as primary care physicians, and specialists such as cardiologists. We also need more clinics so that people have a place to go. A patient may see CDC's wonderful awareness campaign, but in Florida, there's really no place to go for treatment.
The way to remedy the situation is through establishing centers of excellence, said Ms. Soliday. Patients would have a place to go for treatment, doctors would have a place to call for information, and systematic training could be provided for future and existing healthcare providers. The knowledge already exists to provide a lot of diagnosis and treatment. Now research is needed. Ms. Soliday expressed hope for a cure so that Kristin can sit again at the dining room table and do her calculus.

Angela Linford, OFFER member

Ms. Linford had traveled from Salt Lake City to take part in the CFIDS Association Lobby Day on May 15, 2007 and to testify before CFSAC. She told the committee that she came on behalf of not only herself, but the 125 individuals who signed a petition and donated money for her to travel to Washington. She is 28 years old, single, and facing unemployment and loss of health insurance.

In January 2005, she was a recent graduate of the University of Utah, half way through the first year of her career in public affairs, and training for a health marathon. On a Tuesday evening in the second week of January, she went to a spinning class as part of her training and felt the adrenaline high after a challenging workout. Over the next two days, she woke with an increased feeling of pain and a strange feeling of fatigue uncharacteristic of her exercised body. By Friday, she was unable to attend work as she lay in bed fading in and out of consciousness.

After six months, she received a diagnosis of CFS. She had held a public affairs position for a state agency in Utah. She worked full time for 10 months until she could no longer do so. Her supervisor agreed to give special permission for her to work less than 40 hours per in her management position until last fall, when she hit a wall and could no longer sustain even those part time hours. She took FMLA [Family and Medical Leave Act] leave during the winter to seek medical treatment and rest, with the intent to return to work part time for two weeks, then return full time, a requirement for her to retain her position. She was physically unable to work 40 hours. She has submitted a request for accommodation under the Americans with Disabilities Act for a part time schedule, but her current position cannot be done part time or through job share and there are no current part time openings. Legally, the department that she works for has to terminate her. She has been offered a part time position as a private contractor with a consulting firm that does not offer health insurance. The problem that she and many people like her face is that she can work part time, but is unable to get health insurance. She does not qualify for long-term disability because she is able to work, and long-term disability in Utah is only offered to those who cannot work at all. She described her chances for getting Social Security as slim because she is young and the waiting period is usually 3 years. Her medical expenses after insurance are $700/month. She moved back in with her mother during her medical leave and has been supported ever since by both her mother and father.

Patricia Fero, Wisconsin CFS
Accompanying Documents: *NIH Funding Panel – IACFS/ME 2007*
CO-OP For Services

Ms. Fero commended the work of CFSAC and expressed the wish that meetings could be made more available to those who cannot travel to Washington, DC.

- She recommended that CFSAC send two voting members to the Center for Scientific Review sessions where NIH is discussing amending its peer review process.

- She developed a proposal for a national CO-OP for information. The purpose of the co-op is to find misdiagnosed and undiagnosed patients and connect them with the CFS patient community and advocacy groups as well as provide them information and find them services. She is requesting support from the CFIDS Association as well as from OFFER. She has gotten telephone commitments from seven people to be founders and has mailed out 40 information packages. When mis- and undiagnosed patients are found and connected, it may create a groundswell and trigger a “need to know” more about CFS, she said. The cost to pilot the CO-OP will be minimal, but it will take collaboration among CFS networks and patients.

- She suggested that CFSAC explore how to get more information into doctor’s offices.

Cort Johnson, Web Master, *CFS Phoenix website*
Publisher, *Phoenix Rising newsletter*

Mr. Johnson said that watching the progress of CFS research right now is a bewildering experience. There is a sense of researchers being on the cusp of something big and talk of coherence and synthesis. Japanese researchers have mounted a major effort on CFS that is bearing fruit, and the CDC's press campaign seems to have garnered CFS real legitimacy.

The air of promise is not reflected at HHS, where funding does not match the increasingly promising research findings, according to Mr. Johnson. He said that seven years ago, NIH was funding three research centers and a research grant program. At their peak, the centers produced 14 studies a year. Now NIH has trouble funding more than a few studies a year. As the legitimacy of CFS becomes more apparent outside of NIH, it appears that its legitimacy within NIH has declined, he said.

Mr. Johnson cited the neural immune RFA as an example, saying that only about $1 million—or one fourth of the available funding—went to projects specifically focused on CFS. Mr. Johnson expressed particular concern with NIH's decision not to continue funding the research of Dr. Andrew Lloyd, who is studying the physiological changes as people come down with CFS following an infection. Mr. Johnson said that this lack of funding indicates that HHS has not gotten the message about CFS. Instead of administrators determining the focus of CFS research, researchers need to do so, he said. He concluded that NIH needs to do for CFS what it does for other diseases—fund CFS research centers run by CFS researchers who are committed to exploring the multi-systemic nature of the disease to give CFS the legitimacy that CDC's own studies have demonstrated that it has.

Committee Member Q&A

CFSAC members commended the courage of those who traveled to the meeting to testify, often at a risk to their health, and said that the presentations serve as inspiration and reinforce the importance of the committee's work.

Dr. Papernik: There are two things that I think are important for us to take away from these presentations:

- Despite the awareness program, in some states, there is no place for CFS patients to seek treatment.
- There is a striking similarity in the experiences of the people here. While CFS may be multi-factorial, it comes down to a very cohesive picture, indicating that there may be unifying ideology.

Mr. Newfield: We share your concerns about the funding issue and we are looking to accomplish some results in that regard. I also want to bring back the issue of access to the public. We have a paltry amount of live bodies. While the advocates can take back the message, it is important that the community have better access to this forum.
Dr. Desi: It is true that for younger individuals, especially those who are highly educated and who can work part time, it can be difficult to obtain social security benefits. Two pieces of advice—make the application anyway and get somebody who is knowledgeable to help you write the application. You have a better chance of getting a favorable decision sooner if you detail those items in the medical support part of your record that will go directly to your inability

to work. Statements from you doctor really don't help at all. It is important to write and structure the application and cover letter well. Books are available to assist you.

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

Committee Business

Dr. Desi clarified his advice to CFS patients applying for Social Security. He said that a person must be currently insured to be eligible. People who are insured on the date that they apply will continue to be eligible even if they lose their insurance after that date. He also said that part time workers can earn approximately $900 per month and still be eligible. Finally, those who require a wheelchair fall under the category of "inability to ambulate effectively," which is one of the basic criteria for an allowance. Those who need a wheelchair or walker should document it and focus on it, as well as problems with cognitive functions.

Mr. Newfield expressed concern that the committee would become bogged down by wordsmithing in its attempt to compose the invitation letter to third party payers. He suggested that the letter be approved in general (see p 70), then disseminated among members after the meeting to finalize the wording. Committee members read the letter and agreed that it would be disseminated via email for editing and consensus. The intent is to invite third party providers that offer both medical and disability coverage to the next full CFSAC meeting to discuss payment issues related the health care costs.

Committee Recommendations

Mr. Newfield requested an update on what actions have been taken in response to the committee's four core recommendations from the November 2006 meeting. [These appear on page 49 of the meeting minutes.] Committee members agreed that recommendations #2 and #3 had been addressed:

2. ***The Committee recommends that the FY08 and 09 budgets of the CDC for CFS public awareness education be restored to or increased beyond the FY06 level based on the positive initial response to the November 2006 campaign launch.***

3. ***The Committee recommends that CFS be included in the Roadmap Initiative of the NIH.***

Mr. Newfield opened discussion on whether or not the committee wanted to carry forward recommendations #1 and #4:

1. ***The Committee recommends that the FY08 and 09 budgets of the CDC for research be restored to or increased beyond the FY05 level in order to sustain the CDC's remarkable momentum including the ability to finish the Georgia Study (especially the longitudinal portions).***

4. ***Based on the positive response to the NIH's Request for Applications (RFA) issued in July 2005 (funded in 2006), the Committee recommends equivalent funding for a second RFA.***

Dr. Oleske noted that rather than increasing CDC research funding as the committee recommended, NIH has cut it by half. **Dr. Jason** said that the research subcommittee has a new recommendation that addresses the research funding situation.

Dr. Oleske noted that the funding for an RFA recommended in #4 has not been established. **Dr. Hanna** said that the item had been addressed by Dr. Krensky in his description of OPASI. She said that without new money, there isn't going to be anything new and that is the reason to encourage people to apply under new OPASI programs. **Dr. Jason** said that the research group also addressed this issue during its discussion and has come up with a related recommendation.

Clinical/Research/Education Centers

Dr. Oleske returned the discussion to Dr. Klimas's research proposal. Noting that she had edited the recommendation to explain in more detail the problem to be addressed, broadened the recommendation beyond NIH, and made a stronger research center statement, she read her proposal. The ensuing discussion focused on urging the HHS Secretary to draw upon any funding that is available, either now or through new programs.

Dr. Papernik noted that CFSAC has repeatedly asked for centers and been turned down due to lack of funding. Dr. Oleske noted that five out of six public witnesses made unsolicited statements calling for centers and that CFSAC should continue to make the recommendation because it is a priority of the CFS community. **Ms. Artman** commented that although the committee may be asking for the same thing and may be turned down, it is asking in a whole new way that states why CFSAC makes the repeated request.

Dr. Jason suggested that CFSAC might be more strategic about its recommendations by choosing to spend time on only the most important. If centers are the most important priority, the committee should continue to make it the focus. **Drs. Hanna and Willis-Fillinger** noted that *ex officio* members have consistently provided information over the years on funding resources available to the HHS Secretary and suggested that new members access minutes from previous meetings to examine those reports. A summary of available government resources might be helpful as the committee pursues this issue, they said.

Mr. Newfield asked whether the committee could request from the HHS Secretary a summary of funding earmarked for CFS over the years with the idea that if it reveals a decrease, that may provide even more impetus to ask for more. **Dr. Parekh** replied that if there are specific questions that the committee has about the resources of the operating divisions of the department, it could pose those questions to him and he would consult with the *ex officios*. Even if the information has been provided, it could be better collated. Specific questions would be helpful, said Dr. Parekh.

A debate ensued over whether or not an examination of available funding resources might not provide the Secretary "wiggle room" to reject the recommendation. Members modified the last sentence to state that funding be sought from existing or new sources.

The question was called, and CFSAC passed Recommendation 1 (see listing below) by a vote of 8-1. Dr. Hartz voted against the recommendation and Dr. Snell and Ms. Healy were absent.

Education Letter from Surgeon General

Dr. Bateman read the Education Subcommittee's recommendation that the Surgeon General send a letter to state, professional, and education organizations informing them about CFS resources, including the CDC toolkit.

While **Dr. Parekh** prepared the recommendation for discussion, the committee took up whom it would invite to the next full meeting. **Mr. Newfield** noted that while the group has discussed inviting third party payers, Dr. Klimas placed importance on also having the VA give a presentation. The third party payers could take up half a day, said Mr. Newfield, and the group should discuss what to schedule given the time constraints. **Dr. Jason** inquired how much could be accomplished with the groups both before and at the meeting.

Ms. Artman noted that as a CFS patient, her energy level allows more focus on committee business on day one than on day two. She requested that *ex officio* presentations be split between the two days so that the majority of committee business is not saved until the end of the meeting. Committee members discussed ways to streamline *ex officio* presentations, including disseminating PowerPoint presentations in advance and limiting content to new information.

Returning to the November list of invitees, Mr. Newfield explained that his subcommittee has proposed inviting third party providers who cover health and disability claims—Aetna, Cigna, and CMS. Healthcare coverage is the committee's priority, he said, and getting the companies that do both is a good place to start, but he volunteered to research the subject further and come up with a list of more healthcare providers based on coverage of CFS patients. **Dr. Oleske** clarified that the group will invite about three third party providers and ask that they prepare statements ahead of time for the group to digest before the meeting.

Dr. Willis-Fillinger asked if certain providers are more "friendly" than others and more willing to provide a baseline of information. She said that it might be helpful to hear from providers that are already doing some of the things that the committee wants to encourage. Mr. Newfield noted that Blue Cross/Blue Shield in Florida is addressing the chronicity of CFS and may be a good candidate. Ms. Artman said that the list of invitees could be prepared by the Quality of Life Subcommittee.

Dr. Oleske returned the discussion to the recommendation for a letter from the Surgeon General. Subcommittee members read the recommendation, and moved and seconded that it be accepted. The discussion encompassed a possible lack of adequate information sharing at two levels—between state and local health agencies and between state and federal agencies. **Dr. Oleske** cautioned that it may not be wise to address lack of information sharing in the letter because not all entities have that problem. **Dr. Parekh** noted that if the Surgeon General's office accepts the recommendation, the dissemination logistics can be addressed at that time. He also noted that the Surgeon General can send the letter to national umbrella organizations of local health officials.

The question was called and the committee passed Recommendation 2 unanimously (see below).

NIH Review Process

With the NIH grant review process up for change as described the previous day by Dr. Krensky, committee members discussed recommending that the CFS Special Emphasis Panel be used in a demonstration of the new process. Specifically, CFSAC proposed recommending

that the HHS Secretary pilot the review of NIH research proposals in an innovative way similar to the journal review process before their review by the CFS Special Emphasis Panel.

Dr. Hanna suggested that an interim step before a formal recommendation might be sending several CFSAC members to the CSR meeting to speak up and gather information on the review process. **Dr. Parekh** questioned the utility of CFSAC making a recommendation for something that is likely to happen anyway. Dr. Hanna suggested that CFSAC would have more influence if members attended the CSR meeting. **Dr. Jason** took his motion off the table, noting that CFSAC's duty is to recommend, not take action during a process.

CFS Funding Letter

Dr. Jason introduced a third research-related motion to have a letter drafted by the chair to the CDC asking them to specify to CFSAC their current funding and where it goes, plus projected funding for next fiscal year, and specifically what programs will not be funded under a budget deficit. That level of specificity would be extremely helpful, he said. **Dr. Parekh** explained that the committee need not craft the language since the issue will not be put in a recommendation to the HHS Secretary. He and Dr. Oleske agreed to draft a letter, then circulate it to committee members.

Provider Education Resources

The Education Subcommittee requested that relevant HHS agencies report on existing provider education resources (see #2 under Miscellaneous below). **Dr. Parekh** said that the *ex officios* could include such information in their updates at CFSAC meetings. In addition to those agencies represented, the committee added the VA, SAMHSA, and ACF.

Adjournment

Dr. Oleske thanked members of the CFS community for their contributions and diligence in attending the meeting, CFSAC voting and *ex officio* members for generously volunteering their time, and Dr. Parekh for his assistance. The meeting was adjourned.

CFSAC Recommendations/Requests
Adopted at Public Meeting, May 16-17, 2007

CFSAC Recommendation #1

The magnitude of CFS warrants a strong call to action to address the unmet needs of this underserved population. CFS affects at least one million Americans, 85% of whom have not been diagnosed. The degree of functional impairment experienced by CFS patients is equivalent to patients with end-stage renal failure, COPD, and late-state HIV/AIDS.

The CFSAC has listened to public testimony at each of its meetings, and meeting after meeting patients and family members bring heart rending stories of limited access, physicians with no knowledge of diagnosis or treatment, and lives set aside waiting for effective treatment. These lives set on hold translate into an enormous economic impact, with families effected losing half of the household income, costs to the U.S. economy of $9.1 billion per year in lost productivity alone and up to $25 billion annually when medical costs are added to that estimate.

The lack of diagnostic markers and effective treatments, or even treatment guidelines, represents a crisis for evaluation and management of this large population. These factors in combination mandate the creation of innovative measures to focus resources on identifying solutions to these critical problems.

There have been basic science advances which should be leading to new treatment strategies, yet progress in translating these advances into effective treatments has been slow. This is in large part due to a complete lack of clinical care centers and research centers. Investigators are frustrated by a lack of access to representative patient populations, and patients are frustrated by a lack of accessible expert clinical treatment centers. Funding mechanisms to develop new centers for either clinical care or centers for research are shrinking, but the needs of this underserved very ill patient population are unmet and growing.

Therefore, the CFSAC recommends that the Secretary use the resources and talent of the agencies that make up the HHS to find ways to meet these needs. One starting point is our request that the 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. The advisory committee understands that fiscal exigencies have to date prevented the formation of these previously recommended centers, but it is our hope the Secretary will use the full weight of his office to effectively fund this program through existing funding mechanisms that might be available or new programs.

CFSAC Recommendation #2

CFSAC recommends that the Secretary for HHS request the Surgeon General send a letter to state health departments, health professional education programs, national organizations for physicians, PAs, nurses, and other allied health professional groups informing them about the CDC and NIH CFS resources, including the CDC toolkit, CME course and other resources. Members of the CFSAC Education Subcommittee are willing to assist in the preparation of a 'briefing' for the Surgeon General about this matter.

Miscellaneous:

1. Committee requests the Chair and Executive Secretary to use the below language in drafting a letter to third party providers:

"The Department of Health and Human Services Chronic Fatigue Syndrome (CFS) Advisory Committee is evaluating the medical care and rehabilitation of persons with CFS. We are seeking information from 3rd party providers as to classification and coverage for CFS. We are asking representatives of major medical insurance providers to present to the Committee how companies process claims for CFS. Specifically we would appreciate information as to standards for diagnosis of CFS and documentation of associated disability; what treatments are covered and to what extent; and, how rehabilitation and disability are assessed and covered.

We would like to invite a representative of your company to provide the Committee a presentation as to how your company addresses these issues.

2. Committee also requests a report from each relevant HHS agency on existing resources and programs for provider education that might be useful in disseminating information to providers on CFS diagnosis and management.