CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE

Meeting

Wednesday, November 28, 2007
9:00 a.m. to 5:00 p.m.

Thursday, November 29, 2007
9:00 a.m. to 3:30 p.m.

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

Agenda Wednesday, November 28, 2007

9:00 a.m.	**Call to Order**	p 6	Dr. James Oleske *Chair, CFSAC*
	Opening Remarks **Roll Call, Housekeeping**	p 6 p 6	Dr. Anand Parekh *Designated Federal Official*
9:30 a.m.	**Updates from CDC – Research and Awareness Campaign Update**	p 9	Dr. William Reeves, CDC Dr. Fred Fridinger, CDC
10:15 a.m.	**Update from NIH – New Research and Grant Workshop**	p 20	Dr. Eleanor Hanna
10:30 a.m.	**Break**		
10:45 a.m.	**Other Federal Sector Updates**	p 23	*Ex-Officio* Members, CFSAC
11:15 a.m.	**Subcommittee Breakout Discussions**		Committee Members
12:00 p.m.	**Lunch**		
1:15 p.m.	**Subcommittee Updates (30 minutes each)**	p 25	
	1. Education	p 25	Chair Education Subcommittee
	2. Research	p 29	Chair Research Subcommittee
	3. Quality of Life	p 32	Chair Quality of Life Subcommittee
2:45 p.m.	**Break**		
3:00 p.m.	**Update – Peer Review Activities and Initiatives at the Center for Scientific Review**	p 36	Dr. Cheryl Kitt, Deputy Director, Center for Scientific Review, NIH
4:00 p.m.	**AHRQ Report**	p 41	David Atkins, Chief Medical Officer, Center for Outcomes and Evidence, AHRQ

4:30 p.m.	**Public Comment**	p 44	Public
5:00 p.m.	**Adjournment**		

Agenda Thursday, November 29, 2007

9:00 a.m.	**Call to Order**	p 50	Dr. James Oleske *Chair, CFSAC*
	Roll Call, Housekeeping	p 50	Dr. Anand Parekh *Designated Federal Official*
9:15 a.m.	**Benefits and Claims CMS**	p 50	Dr. Jyme Schafer
10:15 a.m.	**Public Affairs**	p 55	Prudence Goforth Director, Web Communications and New Media
10:45 a.m.	**Break**		
11:00 a.m.	**Subcommittee Breakout Discussions**	p 57	Committee Members
12:00 p.m.	**Lunch**		
1:00 p.m.	**Committee Discussion**	p 60	Committee Members
3:00 p.m.	**Public Comments**	p 63	Public
3:30 p.m.	**Adjournment**		

U.S. Department of Health and Human Services

CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE Meeting

November 28-29, 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
Acting Deputy Assistant Secretary for Health
(Science and Medicine)
Office of Public Health and Science

Invited Speakers

Dr. Fred Fridinger, DPH, CHES, Health Communication Specialist, CDC National Center for Health Marketing, and Project Officer on the Public Awareness Campaign for CFS with the Chronic Fatigue and Immune Dysfunction Syndrome (CFIDS) Association
Dr. Cheryl Kitt, Deputy Director, Center for Scientific Review, NIH
David Atkins, Chief Medical Officer, Center for Outcomes and Evidence, Agency for Health Research and Quality
Jyme Schafer, MD, MPH, Office of Clinical Standards and Quality, Coverage and Analysis, Centers for Medicare and Medicaid Services

Prudence Goforth, Director, HHS Web Communications Division

Wednesday, November 28, 2007

Call to Order/Opening Remarks

Dr. James Oleske

Dr. Oleske called the Chronic Fatigue Syndrome Advisory Committee (CFSAC) meeting to order, emphasizing the group's mission of improving the research, provider/public education, clinical care, and quality of life for CFS patients of all ages, races, nationalities, and genders.

Dr. Oleske highlighted reports scheduled for later in the day by CFSAC's Education, Quality of Life, and Research Subcommittees, noting that members' presentations will likely reflect the multiple and extensive conference calls and the hard work that was done since the last CFSAC meeting.

He thanked panel members for their loyalty and expressed gratitude for *ex officio* advisors' outstanding years of professional dedication, citing Drs. Reeves (CDC), Cavaille-Coll (FDA), Eleanor Hanna (NIH), and Deborah Willis-Fillinger (HRSA) for their service. Dr. Oleske commented that he agreed to chair CFSAC because of Dr. Parekh's dedication to the group in arranging meetings and making sure that members stay on target.

Dr. Oleske concluded his opening remarks by expressing gratitude to the CFS community, noting that one of his most difficult duties as CFSAC chair is enforcing the five-minute limit on public statements during meetings. He said that hearing the stories of people with chronic fatigue and their loved ones has been an education for him and has inspired the committee to meet its obligations.

Roll Call, Housekeeping

Dr. Anand Parekh

Dr. Parekh welcomed CFSAC members, conducted roll call, and noted that the committee had a quorum, with 10 out of 11 members present (Dr. Arthur Hartz could not attend). Four out of five *ex-officio* members were present as well (Dr. Laurence Desi of the Social Security Administration was absent). Dr. Parekh added that as a result of feedback from the May 2007 CFSAC meeting, the November agenda included more time for breakout subcommittee meetings and discussion.

Dr. Parekh listed the items that were provided in CFSAC members' meeting folders including:

- The meeting agenda.
- The CFSAC Charter.

- Minutes from the May 2007 CFSAC meeting, which are also posted on the CFSAC website. Dr. Parekh reminded committee members to check the minutes for accuracy before the next day's approval vote.
- The agenda from the *Grantsmanship Workshop for Research on Chronic Fatigue Syndrome (CFS)*.
- Answers from Dr. Walt Hollinger, Senior Medical Director, Medical Operations, BlueCross BlueShield of Florida, to questions posed to him by the CFSAC Quality of Life Subcommittee about coverage for CFS treatments and claims reviews.

Materials submitted by the public including:

- *CFS Patients in the United States Share Their Stories*, a project of the Patient Alliance for Neuroendocrineimmune Disorders Organization for Research and Advocacy (P.A.N.D.O.R.A.) in collaboration with patients and organized by Dr. Lily Chu and Carolyn Field.
- *To the CFSAC Advisory Committee*, a letter in support of the FDA's approval of Ampligen for treatment of CFS submitted by Nancy McGrory Richardson, Education and Outreach Coordinator for Hemispherx, and Anita K. Patton, Reno, Nev.
- *TO WHOM IT MAY CONCERN*, an Ampligen support letter submitted by Linda Barossi, Auburn, Calif.

Dr. Parekh outlined the two-day agenda and highlighted the following:

- Although the committee invited a panel of private and public insurers to talk about quality of life issues and coverage of CFS therapies, only the public payer—the Center for Medicare and Medicaid Services (CMS)—sent a representative to discuss benefits and claims.
- The agenda has been somewhat streamlined in response to feedback that the May CFSAC meeting incorporated too many presentations at the expense of member discussion.
- Dr. Willis-Fillinger agreed to serve as the co-Designated Federal Official during the meeting to fill in for Dr. Parekh when he steps out to attend to other duties.

Dr. Oleske asked committee members to introduce themselves:

Dr. James Oleske, pediatrician specializing in treating children with AIDS and active in advocating for adolescents with CFS as a group that has not received adequate attention. Dr. Oleske said that he has been honored to chair CFSAC, is proud of the accomplishments at the May 2007 meeting, and hopes that the November meeting is equally productive.

Dr. Deborah Willis-Fillinger, internal medicine physician who has worked at HRSA since 1990 and who developed programs for community health centers before coming to the agency. Currently works in the Center for Quality where the emphasis is on evidence-based practice and developing clinical performance measures.

Dr. Marc Cavaille-Coll, Lead Medical Officer, Division of Special Pathogens and Immunologic Drug Products, one of the FDA divisions that review products for CFS.

Dr. Christopher Snell, professor and researcher, University of the Pacific, who has been involved in CFS research for 10 years and is focusing on the functional assessment of CFS.

Dr. Morris Papernik, Chicago internist who treats CFS patients in his practice.

Dr. Eleanor Hanna, Associate Director for Special Projects and Centers at the Office of Research on Women's Health (ORWH) in the NIH Director's Office. Has been involved in government service since she worked as a consultant for the National Institute on Alcohol Abuse when it was instituted in the 1970s. Previously served as Director of the alcohol clinic at Massachusetts General Hospital. Currently heads the CFS program at ORWH and co-directs several other interdisciplinary programs.

Dr. Leonard Jason, psychology professor, DePaul University, and Vice President of the International Association of CFS/ME (IACFS/ME).

Dr. William Reeves, CDC representative.

Kristine Healy, family practice physician assistant (PA) working in the Cook County [Illinois] Bureau of Health Services. She is also a PA educator and Assistant Professor at Midwestern University where she talks to students about chronic diseases such as CFS. She developed her expertise in CFS through working on the CDC/CFIDS Association provider education project.

Nancy Klimas, University of Miami professor, President of the IACFS/ME, and clinical immunologist for more than 20 years.

Jason Newfield, New York attorney who advocates for disability claims for most conditions and considers CFS one of the more challenging illnesses for obtaining payment.

Dr. Ronald Glaser, EBV virologist (virus hunter), Ohio State University Medical Center, who has worked in CFS since the 1980s. Director of the Institute for Behavioral Medicine Research at Ohio State University Medical Center, where a 19-member interdisciplinary group studies stress, blood viral latency, and inflammation.

Dr. Lucinda Bateman, general internist and clinician, Salt Lake City, whose practice focuses entirely on the diagnoses and management of chronically fatiguing illnesses.

Rebecca Artman, CFS patient, Florida, representing the patient community on CFSAC. Performed advocacy work before serving on the committee.

Dr. Parekh, an internist by training, has worked at the Department of Health and Human Services (DHHS) for two and a half years. Previously worked at Johns Hopkins Hospital.

Dr. Oleske again noted that CFSAC had looked forward to hearing from representatives from both public and private health insurance providers about the financing of health care,

treatment, and quality of life for CFS patients. It is somewhat telling, he said, that after repeated efforts, committee members could not convince private insurers to attend. Dr. Oleske said that such behavior reflects the lack of importance given CFS. BlueCross BlueShield of Miami provided a written response and he urged CFSAC members to read it.

Updates from CDC – Research and Awareness Campaign Update

Dr. William Reeves, Chief, *Viral Exanthems and Herpesvirus Branch*
National Center for Infectious Diseases
Accompanying Document: *CDC CFS Program Update November 2007*

Dr. Reeves noted that he would be talking primarily about updates to the scientific program while Dr. Fridinger would discuss public awareness.

Researchers regard CFS as a complex illness, not a simple entity. The illness CFS represents changes in many bodily systems and requires a systems biology approach. CFS is not the result of a single mutation or single environmental factor. The illness arises from the combined action of many genes, environmental factors, and risks. Understanding how the CFS works may lead to elucidating common pathways to other complex diseases.

What do we know about risk factors?

CFS is primarily an illness of adults, although children get it and it's devastating to them. A graph based on data from the CDC's current population studies in Georgia shows that CFS peaks in the 40-59 age group.

CFS is also primarily an illness of women, although men also get it. Georgia study data show that a little more than 5 percent of the population of women report undiagnosed "CFS-like" illness compared to about 2 percent of men. This represents a three-fold excess risk for women. When CFS is stringently defined, about 3 percent of women report the illness compared with about 2 percent of men, with women at a two-fold excess risk. This is clear in virtually every study. Women are the highest risk population.

The data pose a pivotal question: Are the results due to sex (the fact that women have two X chromosomes and men have one X and one Y—primarily a genetic influence) or do they reflect gender? Gender is described as women's role in their particular racial/ethnic group and society; the ways in which they have to function differently because they are women.

The Georgia study is a survey of metropolitan (Atlanta), urban (Macon), and rural populations. Although women generally have a two-fold excess risk, women in the metropolitan population have an 11-fold excess, while the prevalence in men is much lower. In the urban population, it's about 2 to 1. In the rural population, there is an excess in men. These differing risk levels seem to be gender effects.

CFS is highly associated with stress over the lifespan as shown by data from the CDC's Wichita study and confirmed in the Georgia survey. People with CFS are six times more likely than those who are well to have suffered severe childhood trauma, primarily sexual and emotional abuse and emotional neglect. People with CFS also have about a six-fold excess of allostatic load—a physiologic marker of accumulated stress and inability to adapt to it over a lifetime. This shows that CFS may represent an adaptation disorder promoted by early adverse environmental insults. Childhood abuse, infections, malnutrition, and surgeries all are adverse experiences. Over a lifetime, this may lead to a failure to appropriately compensate in response to ongoing challenges.

What do we know about the pathophysiology?

CFS Cognitive Function

Virtually everybody with CFS complains about problems with memory and concentration. But using CANTAB [the Cambridge automated neuropsychologic test battery, a language- and culture-free measure of the major domains of cognitive function], we found in both Wichita and Georgia that there is no difference between CFS patients and well-matched controls in their reaction time for making decisions, the accuracy of pattern recognition memory, their spatial planning, or their rule acquisition and reversal.

Those with CFS do have significant slowing in simple movement time and choice movement time, significantly worse performance in sustained attention tasks, less efficient spatial working memory search strategy, and fewer correct choices in spatial recognition tasks. These are not abnormalities, but they are consistent differences. They are subtle but highly significant. This suggests to us that the cognitive domains and neurocircuitry that link the frontal cortex and basal ganglia may be part of the neuropsychological changes of CFS.

Most people with CFS complain about problems with sleeping, particularly problems sleeping through the night and getting a refreshing sleep. We haven't replicated this yet in Georgia, but in the Wichita study, CFS patients did not manifest any sleep-related disorders. They did not have characteristic polysomnographic architecture and they did not have increased sleepiness, either measured objectively by the multiple sleep latency tests or through a questionnaire. People with CFS did perceive poor sleep quality—significantly more than the well-matched controls. Those with CFS also reported their sleep behavior much more precisely. For example, they more accurately perceived their dreaming and how long it took them to fall asleep.

We extended this study to looking at a spectral analysis of the delta, theta, and alpha waves during sleep. Alpha power, typically associated with quiet waking, was significantly reduced in people with CFS, especially in REM, the sleep period during which the brain is most metabolically active. Again, the level was not abnormal, but significantly reduced compared with the well-matched controls.

Delta power, which is typically associated with sleep homeostasis, was also significantly reduced. We're continuing to look at these results and will have a workshop at one of the upcoming sleep meetings to discuss their implications.

CFS Autonomic Nervous System

Those with CFS have significantly faster heart rates and heart rate variability, significantly lower plasma aldosterone, and higher plasma norepinephrine. This suggests to us that there is a parasympathetic predominance in the sympathetic neurosystem response that may be involved in the pathophysiology of CFS.

CFS Stress Response

Is hypocortisolism a precursor to CFS? Results replicated in Wichita and Georgia show that CFS is associated with a flattening of diurnal cortisol. Salivary cortisol is a measure of physiologic stress response. The first big stress of the day for most people is waking up. Salivary cortisol peaks, then declines through the day. For those with CFS, the awakening morning response is significantly lower and it declines more slowly throughout the day. Again, these show normal but significantly different results.

We have seen in Georgia that this effect is limited to women and to those CFS patients who had significant childhood trauma. This suggests to us hypothalamic/pituitary/adrenal (HPA) axis activity. It may also partly help explain the higher prevalence of CFS in women, and leads us to ask whether hypocortisolism is a pre-existing risk factor.

HPA Axis

An examination of gene expression profiles from the Wichita study suggests that the pathophysiology of CFS likely involves the HPA axis. CFS is also associated in the Wichita study with polymorphisms in genes that involve the HPA axis, particularly the adrenal component of the HPA axis.

Neurogenic stress (such as being nervous about public speaking, being afraid of a repeated beating, fear of being restrained, and anticipation) is generally perceived through the frontal part of the brain. Physical stress (infection, hypothermia, bleeding, and hunger) primarily comes up through the brain stem. But these stressors are mediated through the hypothalamus. Immune mediators and neurotransmitters are involved. The HPA axis is primarily involved in cortisol, has a feedback loop, and influences various systems affected by the other components.

To summarize the current CFS paradigm:

- **CFS represents alterations in complex homeostatic systems.**
- **CFS reflects physical and psychological stress over a lifetime.**
- **Adaptation to cumulative stress alters the normal stress response system.**

The CDC is doing a study collaboratively with Emory University General Clinical Research Center (an NIH-supported GCRC) entitled “Pathophysiologic Mechanisms of CFS: Neuroimaging, Neuroendocdrinology & Genomics”. It is a population-based study using the people identified in 2005 in rural, urban, and metropolitan Georgia:

- A random digit dial was done to 11,000 households.
- We ascertained the health status of the 19,000 18-to-59-year-olds who resided in those households.
- Any adult that was chronically unwell with fatigue had a 30-45-minute computer-assisted telephone interview (CATI).
- Researchers interviewed a similar number of “chronically unwell” (any symptoms of unwellness for at least six months) and a similar number of people identified as “well” by the respondent.
- 6,000 CATIs were conducted with 2,000 well and 4,000 unwell people (2,000 with fatiguing and 2,000 with non-fatiguing illnesses).
- Individuals identified in that round of interviews as meeting the case definition of CFS over the phone were invited to a clinic in Atlanta or Macomb for all-day evaluations.
- Of the 783 people who came to the clinics, 282 had an exclusionary condition (a disease they did not know that they had when we talked to them over the phone).
- Of the remaining 501 people, 124 were well, 113 had CFS, and 264 were unwell.
- In order to participate in the GCRC study, people have to have had CFS and have to be free of medications or come off of their medications the week before the study. Thirty people with CFS and 60 who are well have qualified for the study. The first subjects are scheduled to enter the GCRC study in early January 2008.

The GCRC study will have two parts:

Cognitive Impairment and Mental Fatigue

Day 1: Identify brain regions associated with mental fatigue, cognitive function, and autonomic nervous system (ANS) changes through functional magnetic resonance imaging in relation to the various domains of cognitive functioning. There are reproducible changes in the brain during stress testing which we believe, along with some other studies, may differentiate CFS from non-CFS. We’re very interested in the basal ganglia, particularly the striatal area, which is highly connected to the prefrontal and frontal cortex.

Day 2: Characterize brain structure/function in response to stressful working memory tasks. Imaging will capture changes during stress tests involving psychomotor speed, working memory, and sustained attention. We’re also measuring salivary cortisol, heart rate and heart rate variability, and cytokines.

HPA Axis Regulation

Day 3: Administer Trier Social Stress Test, a highly validated and replicable test in order to:

- Characterize neuroendocrine, ANS, cytokine, and gene expression responses.

- Identify peripheral markers associated with those responses.
- Evaluate role of epigenetic reprogramming, early life stress, and mathematical models of the HPA stress response.

Researchers will monitor EKG, heart rate variability, respiration, and galvanic skin response. These samples will allow scientists to see how test results compare with the mathematical model of HPA axis functioning in normal people.

The CDC will begin the second part of surveillance as soon as the Office of Management and Budget (OMB) approves funding, hopefully in January or February 2008.

- This study will take a population-based approach to looking at the clinical course of the illness; changing morbidity; economic impact; incidence; knowledge, attitudes, and beliefs (KAB); and quality of life.
- The CATI will be repeated with the same phone interviewees.
- Those who came into the clinic without out an exclusionary diagnosis will come in again.
- Every new possible CFS case will be brought to the clinic, as well as appropriate controls for the new cases.

In June or July (pending OMB funding approval) CDC is initiating a pilot registry involving providers in Macon.

- The objective is to create a registry in the midst of an area in which surveillance is already being done so that CDC can relate who does and does not go to a doctor.
- The study will also measure how a targeted CFS awareness program changes the KAB of providers and public in the area.
- Finally, the study offers an opportunity to create a registry of patients for clinical studies, which have attracted interest from Emery University and Mercer Medical School. CDC clinics can be used for trials and provider education.

Two sets of practitioners will refer patients:

HMOs, physicians with private practices, and the medical school. These will include general practitioners, internists, psychiatrists/clinical psychologists, endocrinologists, allergists, and those specializing in family medicine, infectious diseases, rheumatology, and gynecology. Also included will be these physicians' PAs and nurse practitioners.

Practitioners of complementary and alternative medicine. These will include physical therapists, acupuncturists, doctors of homeopathy, massage therapists, chiropractors, herbalists, and nutritionists.

Committee Member Q&A

Dr. Klimas asked for more detail on the statistic that CFS patients are six times more likely to have suffered childhood sexual trauma.

Dr. Reeves noted that CDC has seen the same incidence in both the Wichita and Georgia populations. He noted that the CDC studies are population-based while Dr. Klimas' study is clinic-based, meaning that its subjects are people who have sought medical care. Dr. Reeves said that Georgia study measures are validated, highly replicable instruments put together by a psychologist who is an expert in the field. He also noted the high association with the diurnal cortisol response.

Dr. Hanna commended the CDC for using the techniques being developed in NIH's intramural laboratories, noting that Georgia "will be a great replication study." She then asked about the people who were identified as unwell and how they differ. She also noted that some of the excluded subjects, such as alcoholics, are suffering in some of the same ways that those with CFS. Many conditions that are difficult to diagnose appear similar to CFS when compared with well people.

Dr. Reeves: That's basically a problem that we are struggling with right now.

Dr. Hanna: If you had submitted a grant to NIH for this, it wouldn't be funded because you don't have that other group in there. That's why it's more difficult to get studies funded when they're peer reviewed.

Dr. Reeves: It wouldn't be funded because the review panel would say that it was too ambitious and it couldn't be accomplished. The question of unwellness is pivotal. One outstanding feature of the Georgia study compared with others is that while they screened populations for fatigued and non-fatigued, in Georgia we surveyed for well and unwell. We defined unwell as having fatigue or having problems with cognition, sleep, or pain. Those are central to most medically unexplained unwellness.

Dr. Hanna: How do your CFS people differ from those you excluded on some of these very measures? A lot of things that you're studying in the brain have been developed in alcohol and drugs.

Dr. Reeves: I don't know the answer. What to exclude and not to exclude is a challenge in all of these studies. The path of physiology may be the same in other illnesses. We are looking at medically and psychiatrically *unexplained* illness.

Dr. Hanna: My concern is with your neurophysiological levels. A lot of the conditions that you excluded are other brain disorders and a lot of the stuff you're using comes from the investigation of those disorders. Since childhood stress has been raised as a major risk factor for CFS as well as for other conditions—especially in addictions—I think that it's important to know how these excluded groups differ from your CFS group.

Ms. Artman: I have a concern based on the fact that these study numbers may be used by Congress for funding. I am concerned about eliminating people with co-morbid conditions from our count of how many people have CFS. People who develop another illness such as Addison's disease or hyperthyroidism while they have CFS may become excluded from the CFS population.

Dr. Reeves: Close to 40 percent of people who are unwell in the population who meet the criteria for CFS have other undiagnosed diseases that can be treated. The important public health message from this isn't whether those people have CFS, but why they aren't getting medical treatment for something that can be fixed. You can have many conditions and also have CFS. A message to providers is, if you have someone who comes to you complaining about the symptoms of CFS, look at them in some detail, because a significant portion of them are going to have something that you need to treat. The allostatic index is important. It is a predecessor to a variety of things. A high proportion of people with CFS have metabolic syndrome. The message is, don't write someone off once you determine that they have CFS if they develop something new.

Dr. Oleske: One of my concerns is that the treating physicians will frequently hear or make a diagnosis that the patient has CFS, then everything that they would do for that patient stops. I've been amazed, for example, to see how many CFS patients have undertreated asthma. In fact, most of the conditions in CFS patients, in my experience, have been undertreated because everything gets blamed on the CFS and no symptomatic care gets provided. The important message that we have to get out is that CFS patients can be treated, and some of those treatments are related to co-morbid conditions that are usually neglected.

My question is, how long is your surveillance registry project going to run? I happen to be a great believer in how important but difficult it is to fund long term follow-up. Why go to the trouble of registering and having patients in surveillance and collecting all that important data, then not follow them for a period of time that would be reasonable—certainly more than four or five years. How long are you going to try to follow them?

Dr. Reeves: It depends what we see. As long as we are seeing changes and we can follow them, we plan to do so. We also plan to expand this to a less intense regional registry. We would continue as long as there is money and as long as we find changes. One of the nice things about CDC or NIH is that we can do longer-term observations.

Dr. Oleske: One major issue that I think your data is pointing out is that there is room for clinical trials as you develop these registries. Those populations that are well defined would be able to fit into clinical trials, if only we had the structure to do them.

The technology available is amazing. For example, researchers were able to determine with a PET scan that some people in a vegetative state responded dramatically to Ambien—a paradoxical response. The scan showed that their frontal lobe became active—and complete loss of frontal lobe functioning is the problem in a complete vegetative state. The ability to measure function and activation of the frontal lobes is a perfect way of looking at the screening of drugs that could be used in a clinical trial.

Dr. Jason: In our community-based trial in Chicago, we did not find that association between the types of early trauma and CFS/ME. One always needs to look at several different samples to make these types of conclusions. My question has to do with prevalence numbers. I noticed on your slide that from ages 30-39, it seemed like four percent of

individuals had CFS, and yet in the general population, the overall slide was 1.7 percent. The reason that I ask this question is that in published literature, the actual rates are a little bit higher than that. Have the rates decreased in the Georgia study from what had been published? The empiric case definition developed by the CDC differs from the more traditional clinical evaluation. What implications does this have for both the rates that had been reported as well as the current, possibly revised, rates that you've shown?

Dr. Reeves: The 1.7 is the relative risk of women to men, not the prevalence. The prevalence in Georgia is 2.54 percent. That has not changed. The question of how one defines CFS is a question that everyone has struggled with. The problem in my mind with the 1994 case definition, which most people apply in research, is that when you ask somebody, "Are you fatigued, yes or no?" it is a meaningless question. Eighty percent of respondents in one study of medical residents did not know the difference between fatigued and sleepy.

In the 1994 case definition, the fatigue must cause significant impairment in one's usual occupational, educational, social, or recreational activities. But many people with CFS don't find the fatigue their biggest problem; they find the fact that they can't think straight their biggest problem. It isn't the fatigue that impairs them, it's the illness.

It was the consensus of an international collaborative group in which a high proportion of the best CFS investigators in the world participated that:

- In research studies, reproducible criteria need to be used.
- It is the impairment due to the illness that needs to be measured.
- That impairment needs to be measured with an instrument that is relatively standardized and replicable in all studies.

If that instrument and those scales are used in all studies that a group does, they will identify the same levels of fatigue independent of where the population is. On the telephone surveys, we screened using the 1994 definition verbatim. Those perceptions are not replicable, but when I bring respondents into the clinic and use the standardized instruments, I know I can replicate.

Dr. Klimas: We heard a conclusion from a CDC blue ribbon panel at our May 2007 meeting that CDC should be developing new interventions. I didn't hear in the future directions part of your presentation that this is on your game plan. What is status of your future funding and how will you spend it?

Dr. Reeves: We are going to put on a workshop in spring 2008 to talk to investigators and clinicians about interventions. We want to use the clinic in Macon, although we don't have concrete plans. I cannot answer the funding question. Funding answers need to come from the financial management office of CDC. Our current funding, projected from the continuing resolution is slightly less than it was last year.

Dr. Oleske said that he would gather CDC funding information by the next CFSAC meeting.

Dr. Fred Fridinger, Health Communication Specialist, *CDC National Center for Health Marketing*, and Project Officer, *Public Awareness Campaign for CFS with the CFIDS Association*

The CDC national public awareness campaign is targeting those at risk for CFS and primary care professionals. The secondary target is general awareness of CFS. All messages and materials for the campaign go through various types of qualitative research and testing. The theme is identifying risks and symptoms in individuals. The call to action is for individuals to identify symptoms. We are also trying to raise awareness of the importance of diagnosis and treatment and convey that this is credible information coming from HHS and CDC.

Public awareness campaign components:

- November 3, 2006 – Media launch at National Press Club in Washington, DC
- November 3, 2006 - Satellite launch

Throughout the following year:

- Media tour to reach those who could not make the National Press Club release
- Print and online ads
- Public service announcements for TV and radio
- "Faces of CFS" traveling exhibit
- Printed patient brochure and provider toolkit on CDC and CFIDS websites
- Media outreach and partnerships with various organizations of healthcare professionals

Media Coverage

- Over the past year, the media has given CFS more recognition as a serious disease and public health issue. As of October 1, 1,800 stories/articles have appeared as a result of the awareness campaign. CFS materials have garnered 200 million media impressions (viewings). Eighty-two percent of stories treated CFS as a "real" or "serious" condition.

- The "Missing My Life" public service announcement (PSA) was distributed to 800 stations and has garnered more than $2 million worth of combined TV and radio air time. Although the PSA is still in the top 45% most popular, play time has dropped recently. We plan to do a mailing to remind the media about the PSA and provide them another copy if needed.

- Mainstream magazines—*People*, *Ladies Home Journal*, and *Better Homes and Gardens*—have run seven full-page campaign ads and web banner ads run on the sites of these magazines as well. CDC has gotten media requests to incorporate the ad into news stories.

Plans for FY2008

- CFIDS Association will coordinate the traveling Faces of CFS exhibit with interviews in the major and ancillary suburban media of the cities in which the exhibit appears. It is scheduled to appear at the CDC Washington office in December, accompanied by a media event highlighting CFS as a public health issue. Atlanta physicist and CFS patient Wilhelmina Jenkins is scheduled to attend the event. The exhibit will also travel to annual conferences of relevant organizations.

- Printed materials (which appear on both the CDC and CFIDS website) are being updated.

- The awareness campaign is deemphasizing paid media and focusing on earned media (inspiring a story without paying) in conjunction with the traveling exhibit.

Survey Results

KAB data from 2007 has been tabulated recently from an omnibus mail out survey of the public and primary care practitioners that included questions about CFS. The public survey was conducted with a panel of roughly 5,000 American adults weighted to the U.S. census:

- 57 seven percent of respondents have heard of CFS.
- When responses of "strongly" and "somewhat" are combined, 45 percent agree that CFS is a debilitating disease.
- A little more than half of respondents strongly agree or agree that CFS affects people of all races.
- One in 10 people said that they had read or heard about CFS in the past few months. This survey is not an instrument sensitive to the awareness campaign, but it does indicate that awareness of CFS has increased, particularly for the general public.

Responses from 1,500 primary care providers show that:

- 96 percent have heard of CFS.
- 30 percent said that there is enough information available to diagnose CFS.
- 90 percent said that CFS can impair quality of life.
- 20 percent strongly or somewhat agreed that CFS is only in the patient's head.
- 15 percent had read or heard about CFS in the past few months.

Committee Member Q&A

Dr. Jason: There's actually a validated instrument called the chronic fatigue attitudes test (CAT) that you might want to look at. My question has to do with Rich Carson, CFS patient and founder of ProHealth, Inc., who is launching a large-scale effort with media personalities and patient advocates to get the name of the disease changed to MECFS with ME standing for either myalgic encephalopathy or encephalitis. Are you aware of this and do you think that it may affect the work that you're doing?

Dr. Fridinger: [Stated that he is not aware of Rich Carson's work.] From a communication perspective, making changes related to messages and what people call things adds complexity. Although I'm not totally convinced that CFS is in the public's consciousness, this would be enough to confuse them. It could also make a difference to patients and healthcare practitioners.

Dr. Reeves: I have great concern that if 90 percent of providers are saying that they know about CFS and it is a serious illness, it will cause problems if we change the name just to change it. I would much rather see groups' efforts aimed at education, treatment trials, and getting at the path of physiology.

Dr. Oleske asked if **CFIDS Association President and CEO Kimberly McCleary** wanted to comment on the name change issue.

Ms. McCleary: Rich Carson and I have had conversations about this topic and how a change to MECFS would affect this campaign. Because the bulk of the launch activities used the term CFS, you'd really have to form a new campaign to reintroduce and redefine the term. It's not as simple as going in and swapping the names. It would be very costly. We would spend all the remaining resources on renewing all the materials.

Dr. Reeves: When we dealt with the 1994 case definition, it took over two years of meetings of invited lead investigators and patient advocates. Changing it again in 2003 was the result of a three year process involving all relevant groups. Those who launched the effort to change the diseases name have not invited anyone from the CDC research group to participate. Just mandating a name change is not how one does it. One does it through very serious and deep meetings that involve experts in the communication and scientific fields.

Ms. Healy: Can you give us a timeline for how long this awareness campaign is funded?

Dr. Fridinger: The campaign is funded through September 2009. The activities included are the dissemination of web and print materials and the PA announcement, and continuing the traveling exhibit and generating related media coverage. The provider education project is funded separately.

Dr. Reeves: The scientific program is responsible for provider education because it involves more technical subjects. It is a continuing activity funded directly through program, not operated as a contract.

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

Dr. Oleske announced that in order to make up time in the meeting schedule, subcommittees would meet for their breakout discussions during lunch. Committee members agreed to the scheduling change.

Dr. Eleanor Hanna, Associate Director for Special Projects and Centers, *NIH Office of Research on Women's Health (ORWH)*
Accompanying Document: *Grantsmanship Workshop for Research on Chronic Fatigue Syndrome (CFS)*

Dr. Hanna: The grantsmanship workshop that we held in September turned out to be extremely successful, especially because two new things were announced there:

- **The Multidisciplinary Program (MAP) for multi-pelvic pain disorders.** I had encouraged the NIDDK [National Institute of Diabetes and Digestive and Kidney Diseases] to get involved in this area because one of our score directors at Washington University studies interstitial cystitis. He was researching the idea that infections are not new, but arise from reservoirs. I remarked that we need something like this for CFS. NIDDK is now funding a program for multi-pelvic pain syndromes. All the conditions are those that could have infectious origins. The NIDDK project director for the program presented at our workshop. He has become a member of our CFS working group.

- I've been working on measuring fatigue with the National Institute on Aging. They conducted a meeting some time ago and invited some CFS researchers. Unfortunately, these researchers were trying to move NIA away from studying CFS and aging because they contended that chronic fatigue is not a disease of old people. The institute does not subscribe to that theory and will soon be releasing an R21 on fatigue and aging. I'm not sure whether ORWH is going to be able to fund it. It would be better for our budgeting if these kinds of studies came in through the CFS announcement rather than the aging announcement, but I am still closely involved. NIA has now become a full member of the CFS working group.

I also invited people from Fogarty International Center (who have joined the CFS working group) and from NIDA. All of the talks and a video tape of the meeting are available on our website (http://orwh.of.nih.gov/cfs/cfsFundingGMWs.html). We put a huge emphasis on the need to do interdisciplinary research because nothing else is going to fly.

According to unofficial 2007 data, there are four newly-funded grants in CFS in addition to the seven we funded last year from the RFA. Of the four that were just funded, two were funded by the National Institute of Nursing Research and are basically treatment grants. One study is a telephone-based treatment and the other looks at a treatment for sleep disorders in CFS. The other two grants are a combination of basic and clinical research more in line with what we funded in the RFA. I'm hoping that this interest will continue and be sustained so that we can add more grants every year.

Other plans for FY2007:

- We did not have the annual meeting of investigators in FY07 because they didn't have enough data to present, but we are planning one for FY08. We will hold a planning meeting in December and another meeting that focuses on treatments or interventions for CFS, including alternative treatments.

- Our PAs [Parent Agreements] have expired and we need to reissue them. I invite people to give me ideas for how they can be changed. You can access them on the website. We're meeting December 20, and I'm hoping that within a month, I can get the new version up The Office of Extramural Research has agreed to keep the old ones alive so people can feel free to apply under these—they're not dead even though the are labeled as expiring on November 4.

I hope that we can continue to work within NIH to foster collaborations and build more in the intramural program.

Committee Member Q&A

Dr. Jason: Nicole Porter at DePaul University just finished a literature review of CFS alternative and complementary treatments and has sent it to a journal. The data out there is not that convincing.

Dr. Hanna: But this is the interest of some members of the committee. It won't be the focus of the meeting, but we've got to look at all the treatments out there.

Dr. Jason: Certainly there are lots of promising things, but that's probably all they are right now…promising. Pediatric issues have been something that there's lots of interest in, particularly in the patient community. How important will pediatrics be in the new announcement in terms of encouraging people to apply?

Dr. Hanna: I think you know from the old announcement that we don't discount the pediatric population. In fact the chair of the RFA review was a pediatrician who focuses on CFS. Any good research proposal that can answer its question will be considered for funding and it won't matter what Institute it goes to. If the Institutes don't have the money to fund it, then ORWH will pick it up. I try to keep a close eye on those when they come through. Another good sign is that the people at NIAID, knowing that the PAs were expiring, asked if we were going to renew them and were happy that the arrangements had been made. They still support CFS research even though they don't support Centers.

Dr. Klimas: The grant writing conference was phenomenal and gave those who attended the opportunity to meet your working group. I was very impressed with their dedication, enthusiasm, and efforts to stretch their mission to encompass ours. My sense of what the Roadmap people said is that it's an either-or thing—if you go the Roadmap route, it takes away from NIH's response to other CFS research. Are we wrong to pursue the Roadmap at this point?

Dr. Hanna: No, not if you have something that fits it. I think that you all got the message that the Roadmap funds infrastructure kinds of things. The entire medical establishment is being retooled to fit the Roadmap model and to encourage interdisciplinary research. My vision is—speaking as a private citizen—that eventually that's where all the research is going to get done: less so in the NIH clinical center and more so out in Clinical Translational Science Award (CTSA) facilities that have been equipped to encompass more collaboration.

I don't think that there will be less research, I think there will be more and that it will involve more of the clinical side of things as well as the basic side of things. I think that we'll continue to have something in the intramural program and maybe that will be the place where you could have first-stage clinical studies being done because they might not be able to get done anywhere else.

I wouldn't discourage you if you have something for the Roadmap, because CFS is a perfect model of something that encompasses all the systems. If you think it would be easier to just submit a research project to get funded by one or two Institutes and us, do that. You know what the Roadmap's about and you know what the CTSAs are about, so it's up to you.

Dr. Klimas: One of CFSAC's recommendations to the Secretary has been to establish five clinical and research centers. I'm still not sure what a funding mechanism might be—how it involves NIH, HHS, or any of its other agencies. How would you advise us to pursue these Centers of Excellence?

Dr. Hanna: The same thing that I've been advising you from day one and that is to take advantage of the Centers that you can apply for and work with the Centers that are funded in the Institutes. I don't think at this time that we're going to get the financial support for CFS centers at NIH. I don't think that the research is there yet. At some point it might be there, maybe after the RFA grants finish. There are lots of opportunities out there. I'm hoping that people will form a collaborative to address CFS in the MAP program.

Dr. Willis-Fillinger: Would you be able to give us a brief discussion of funding at NIH—where the dollars come from to begin with?

Dr. Hanna: The dollars at NIH are not allocated to anything specifically except the Roadmap and anything else that crosses all of the Institutes. There is no funding for CFS research. The only hard funding that exists is my salary. I am chronic fatigue at the NIH. Women's Health pays for that, and they pay for the conferences that we do, even though the other Institutes come in on it. I think it's easier for us to make an impact now that the whole nature of NIH has changed to be more interdisciplinary, because what we do in CFS fits the model more than what people have been doing with individual diseases. CFS spending depends on the number of grants that are funded every year. That's the budget. That's the only money that NIH counts as CFS funding. They don't count what we spend on meetings or my salary. It's just a research budget, so it's what we spend directly in research dollars.

Dr. Jason: For about a 10-year period of time, NIAID was the primary group that was funding centers. In the mid-1990s we certainly knew far less than we do today about some of the

issues with this illness, and at that time there was the clinical will to fund Centers. A number of those Centers did some fantastic work and helped shape the field. If there was the willingness of NIH to fund Centers in the mid-90s for at least a 10-year period when we had far less information, how did that willingness occur then and what types of things might we be able to do to replicate those circumstances?

Dr. Hanna: That's not something that I can answer. It's above my pay grade. But I can tell you that within the new structure of NIH there will be fewer and fewer Centers focused on individual diseases. We got a certain body of knowledge from some of the Centers that NIAID has funded. But then, a lot them just rested on their laurels, and they weren't producing anything that NIAID felt was consistent with the scientific agenda. NIAID's advisory committee recommended that the agency not fund centers them anymore. Nobody else at NIH was willing to contribute because the centers couldn't give us a good accounting of what they had. I still contend that if people form their own collaboratives within the research environment that exists now, you might have something better than you had before. Nancy's group is a very good example.

Dr. Parekh: Lenny, if you or the committee would like more specific information on NIAID, we can always invite NIAID leadership.

Dr Hanna: As with all the other Institutes, they are funding CFS research that fits their mission.

Dr. Oleske: It is important to have a link between research and where people get their care. We essentially eliminated perinatal HIV thought prenatal care. We supported research, but also centers of excellence for clinical care. If we're ever going to be successful in the treatment mode, it must be in the context of where people get their care. Every patient with CFS should be enrolled in a clinical program.

Other Federal Sector Updates

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

I want to bring people's attention to a very important act that was signed by the President on December 27, 2007, the Food and Drug Administration Amendments Act of 2007. The law represents a significant addition to the FDA's authority, including the reauthorization and expansion of the Prescription Drug Users Fees Act, the Medical Device Users Fees Act, and the Modernization Act.

This law is important because a large amount of the funding for the reviews of products right now comes from user fees. This is basically the fourth version of this five-year act that we're receiving now for reviewing drugs. The programs will ensure that the FDA staff have the additional resources needed to conduct the complex and comprehensive reviews necessary for new drugs and new devices.

Two other important acts were reauthorized: the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act. Both of these are designed to encourage more research into and development of treatments for children. I urge you to go to fda.gov to read more detail about these acts. There was nothing specific for CFS in these acts, but CFS will still benefit from the strengths of all the disciplines that can address many of the scientific issues and try to develop treatments for this condition.

Committee Member Q&A

Ms. Artman: *USA Today* had a summary of the new law two days ago. It's very beneficial for summarizing what's going on at the FDA.

Dr. Klimas: Rumor has it that Ampligen is winding its way through the FDA. What is the status?

Dr. Cavaille-Coll: I cannot comment on any status of any application. That is in United States criminal law.

Dr. Jason: For researchers who have interest in this area, are there mechanisms that we could let the greater community know about that are going to your agency to support either conferences or basic research in this area?

Dr. Cavaille-Coll: Unfortunately it's not part of our mission right now to do that. There is an initiative called the Critical Path to collaborate with investigators in industry to identify biomarkers or to validate biomarkers that can be used in all aspects of drug development or finding different ways of adapting trial designs. That's up in the Office of the Commissioner and is not specific to any health area. FDA also has an Office of Translational Science that is helping to coordinate that effort.

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

HRSA supports health professional education and training, direct patient care in a number of different areas (HIV), and other primary care community and rural health centers.

HRSA just celebrated its 25th anniversary. In general, the agency is estimated to care for upwards of 15 million U.S. patients, and there is an accelerated focus on quality improvement and patient safety. We have a number of initiatives of interest to CFSAC:

- **Implementation of clinical performance measures** across the agency targeting all of the programs that provide direct patient care.
- **Implementation of electronic health records.** Less than 10 percent of the facilities in the programs that we fund have electronic health records. There's a real need for the healthcare safety net to get up to speed. We have a number of health center

- **Health disparity and health improvement collaboratives.** These target the high-priority public health areas of diabetes, hypertension, cardiovascular disease, cancer, and HIV and cover both rural and urban populations across our programs.
- **Patient safety and pharmacy.** Collaborative will be launched in Summer of 2008
- **Health literacy**. Training for providers is available.

The agency is moving aggressively in quality improvements and performance measurement. We're looking at specific indicators across all our programs. As more definitive information about the treatment and diagnosis of CFS becomes available, we're ready and willing to disseminate those.

Committee Member Q&A

Dr. Jason: A number of years ago, HRSA had some involvement with the CFIDS Association provider education program. Is anything like that possible in today's climate? How did the contingencies come together for that kind of programming a number of years ago? Could such initiatives occur today and if so, it seems like the research community would be interested.

Dr. Willis-Fillinger: I can take a look at that and get back to committee.

[Dr. Oleske called a break for lunch.]

Subcommittee Updates

Kristine Healy (Chair) reported for the Education Subcommittee

We had several conference calls this summer and lots of email communication as we followed through on the committee's recommendation to draft a letter that we would ask the Surgeon General (SG) to distribute widely to a network of healthcare providers and organizations.

This summer, subcommittee members (Drs. Bateman, Klimas, Papernik, Willis-Fillinger, Reeves, and Hanna joined by Drs. Parekh and Oleske) met over the phone. Dr. Bateman drafted a letter and subcommittee members gave their input. Dr. Parekh arranged for several meetings with the SG attended by Drs. Oleske, Papernik, Willis-Fillinger, and Parekh.

Dr. Papernik: The SG was very receptive and thought that our program was good. He, his science officer, and his assistant had a lot of questions about the definition of CFS, the classification, and how we can get people to believe in an illness that doesn't have a marker. Dr. Oleske and I went over the fact that there are other illnesses with guidelines out there that don't have specific biomarkers, and yet they're treated as if they are "real diseases". The SG

said that he would take our recommendation under consideration. He was the Acting SG at the time and has since retired. He passed on our recommendation to the new Acting SG.

Dr. Willis-Fillinger: There was some discussion with the new staff that picked up the task of pulling together the letter. We provided them some updated information on CFS from the CDC and NIH. Ultimately, the drafting of the letter is in the SG's office.

Dr. Parekh: I think that the reaction of the new acting SG was sympathetic, but brought up several issues:

- He would like to revisit the subject of sending out a letter in the spring because he is just starting his major initiatives and he wants to concentrate on those. My comment to him was that we are only asking for a letter as opposed to requesting that he go out and address the community to raise awareness. The communication staff maintained, however, that if the SG sent a letter to hundreds of organizations raising their awareness of CFS, the community would assume that the SG is going to carry the banner of provider awareness and the office would be deluged by requests to speak at and attend events.

- Subcommittee members are still working with the SG staff on content and discussing whether the letter should raise awareness of CFS by referring recipients to CDC resources or educate letter recipients. Subcommittee members drafted the letter to do a little of both, and there's discussion whether it should be one or the other.

- How can we measure the impact of the letter and maximize its benefit?

- To whom should the letter be sent? Should we be more specific than merely listing several large organizations?

My thinking is that the SG did not give a "no", but I think that between now and spring, there's work that the Education Subcommittee can do with Drs. Reeves and Hanna, who have some ideas about the content.

Dr. Oleske: I was very impressed that they really paid attention to us – not just the SG, but his complete senior staff. They were all in favor at the conceptual level of having the SG's office alert Americans that CFS is an illness that needs to be addressed appropriately. The new person is as sympathetic, but he's just coming in, they have a childhood obesity program, and he really doesn't want to dilute it by coming out with a major statement on childhood obesity *and* CFS.

This whole concept is eventually going to bear a lot of fruit, but there are some simple things that we need to do prior to that such as ask the *ex officios* to make sure that their issues are covered in the letter. Once we get the final draft, the Education Subcommittee needs to look at it carefully and must make sure that it conveys our original intent.

Dr. Papernik: Are there specific points that we should be looking at? Should we wait for direction from the SG before we start working with letter?

Dr. Reeves: What is the objective of the letter? And is there a way that we could see if it made a difference? Is it just to sensitize providers that CFS exists? Ninety percent already know that it does. Do we want to convey ways to treat CFS?

Dr. Parekh: I think it would be helpful while we're waiting to hear from the SG to make sure that CFSAC is comfortable with the content of the letter. It would be helpful if the subcommittee presented the letter in its current form.

Ms. Healy read the subcommittee's November 1 draft.

Dr. Oleske explained that the subcommittee had discussed whether or not to mention nongovernmental websites in the letter. Those who argued for inclusion ultimately compromised and allowed advocacy sites to be removed because both the CDC and NIH websites refer to the major nongovernmental sites.

Ms. Artman: I think that one way you could gauge the effect of the letter is by measuring the increase in the number of hits on the CDC website that go to the physician education tools after the letter is sent. You're doing a measure already. An increase would tell you that more people are seeking information.

Dr. Klimas: Something that should be brought to the SG's attention is including a direct link to the toolkit. If I saw something that said "Physicians Toolkit Click Here" I would click that button. But if I saw it that it was the CDC.gov website, I wouldn't click that button. Or add the toolkit as a separate link. I think that would be more likely to have an impact. I open attachments more than I open links.

Ms. Healy: We had a very clear objective with the letter and that was to link providers to federal resources and information. The public awareness campaign already has a mechanism in place for measuring attitudes and changes. Maybe we can use that as a follow-up after the letter goes out as well.

Dr. Reeves: We are about to begin a very sophisticated analysis of the website that goes beyond whether the hits go up and down. Do people stay on the website, where do they come in from, what are they navigating to, what are they downloading? You need more concrete objectives for this letter. Is the objective to inform recipients that they can get toolkits to help them with their patients? That they can get CME credits that will help them know more about CFS? Those are more concrete objectives that can be measured.

Ms. Healy: That is step two. If they don't go to the website, none of that happens. The purpose of the letter was to direct large numbers of people to a very good resource so that it gets used.

Dr. Reeves: The question from the point of analysis then becomes, is it happening?

Dr. Parekh: Fred Fridinger said before he left that he would be interested in looking at the issue of measurement. I think Fred would be a resource to help us determine exactly how we can analyze if the letter is making a positive effect.

Dr. Snell: If the letter is sent out, will it be in the public domain? Can it be sited? It adds gravitas to other materials if you include something from the SG.

Dr. Parekh: Yes.

Dr. Oleske: The letter would be a great accomplishment for CFSAC. I don't know about you, but when I get a letter from the SG, I tend to read it and take it seriously.

Ms. Healy: It was a wonderful group effort. We have other things that we're going to be working on for tomorrow. We'll certainly want to continue to work on this letter, and given this feedback that we've gotten, we'll think about how to make it more effective and how to measure the outcome. Our other areas of interest include:

- The public awareness program.
- The provider education project. This really has to be strongly continued because once people get this letter, the provider education project is going to be critical. We'd like to see the outcomes of the project for this current year and perhaps by the next meeting, have some information about how the participants are evaluating the program. We want to make sure that the CME content is really working well for the providers. Are they getting enough information about clinical management of patients beyond the epidemiology and diagnosis? Are we actually giving them the tools to care for patients?
- An AHRQ update of the clinical guidelines on CFS. We think that it would be important to let AHRQ know that other organizations have clinical guidelines (IACFSME, for example). Perhaps AHRQ could collaborate with experts from those organizations to shorten the timeline for the update.
- Consider inviting someone from AHRQ as an *ex officio* member.

Dr. Oleske: That last suggestion is excellent. I think that we should listen to what AHRQ has to offer, then consider that. I actually wrote one of their first guidelines and was very impressed with their vigor.

Dr. Klimas: The subcommittee also would like to invite someone from HRSA to the next CFSAC meeting to discuss how one incorporates issues into the curriculum of provider education programs that HRSA is developing.

Dr. Papernik: The CDC and the CFIDS Association were working closely on provider education, but I understand that they will no longer be working as closely.

Dr. Reeves: CFIDS has elected not to bid on the next phase, so we're continuing the effort directly through program. CME accreditation was through CDC's office anyway. The focus

will be on CME for physicians, nurse practitioners, PAs, and allied health professionals. The other big part of the program was outreach to medical schools through grand rounds. That will continue as well.

Ms. Artman: Why didn't the CFIDS association bid to continue as a provider?

Ms. McCleary: (Audience) We were concerned about the type of information that was being provided through the contract and the requirements that would be imposed for the continuation of the contract. The feedback we received and our evaluation measures pointed to the need for more clinically-based information rather than research and epidemiologically-based information. We felt that we would be freer to pursue those initiatives independent of CDC funding.

Ms. Artman: Will you continue to do provider education independently?

Ms. McCleary: (Audience) We will, but probably not all of the aspects that were part of the CDC contract.

Mr. Reeves: I don't think that you can have too many venues for this. I think that the important thing is looking at the outcomes. We did have a very productive seven or eight years with CFIDS. We worked together closely analyzing the results to see what differences were made. We are now tying public awareness and continuing medical education to control of the illness. If CFIDS or other organizations pursue this using a different strategy, we can only all come out ahead, and the patients can only benefit.

Dr. Parekh: My advice for the Education Subcommittee would be to make sure that the letter's content is in line with what we discussed today. I think that everyone agrees on the SG purpose/objective part, but make sure that we all agree on the performance measures and how we're going to evaluate it.

Dr. Oleske commented that the decision to list only the CDC and NIH websites in the letter was not a political one, but a practical one based on the fact that both of those websites list the major CFS interest groups.

Dr. Leonard Jason, Chair of the Research Subcommittee reported;

The panel met by telephone on June 12, July 24, and September 4 to consider:

Understanding how money is coming into the CFS/ME arena and being used. The United States probably has more money available for doing work in the area than any other country in the world, with the possible exception of Great Britain. What happens in the United States is important not only for our citizens but for the world. We thought that it would be extremely helpful for us to get a sense of how much funding is coming in, particularly to NIH and CDC, and how that money is actually being used—what types of grants, what types of activities at the CDC, and what is not being funded due to budget deficits.

Looking at medical schools texts to see how they cover CFS. We're looking at the percentage of pages that contain information about CFS and the quality of that information. We have whole new generations of healthcare people who are being trained and we want to know what they are learning about CFS. We will have information to present to CFSAC at the next meeting. We have spoken to the Education Subcommittee about some of this work.

Looking at the expertise level of the Special Emphasis Panel (SEP) that reviews CFS grants. We have focused questions for the Center for Scientific Review (CSR) official who will appear before CFSAC today including what will happen when the current scientific review officer steps down in May? Will the special emphasis CFS panel continue? Are there a similar number of proposals in this area being submitted when compared with the past? The RFQ was a boon to CFS research, but has the momentum continued? We'd like to find out how many of the incoming proposals get a priority score and ultimately get funded. There is a perception in the external world that it is very hard to get research funding for CFS. Having some data on this would be helpful.

Understanding CDC funding. We have data from Dr. Parekh and previous meetings on CDC funding patterns over the last number of years. We're hoping to compile this information and draw a comprehensive picture. Dr. Hanna has summarized NIH funding, Dr. Reeves has indicated his research needs, and Dr. Fridinger has provided information on the awareness campaign. We have the overall amounts for 2005-07. It's also critical, however, to know what this money is funding. There may be areas that aren't being funded appropriately where we need to make recommendations for increases.

Dr. Ronald Glaser: There are at least two ways that NIH can attract people to do research. Considering that primary investigators (PIs) have to spend a lot of time preparing a grant proposal before submitting it, they need to be attracted to finding new answers to old questions. We have a 20 year history studying CFS and we still don't know what causes it nor have we uncovered biomarkers that can diagnose it. How do we attract people with new hypotheses to come in and to try to find answers to those questions?

One way is with an RFA, and I think that NIH had some success with that. Another way is to assure PIs that when they submit a proposal, it has at least a fair chance of getting a review by people with appropriate expertise. If you don't feel confident that that's the case, you could get discouraged and stop submitting proposals.

We looked at the membership of three different versions of the CFS special emphasis panel. You might assume that people reviewing grants have the expertise to do so. We measured that expertise based on the following criteria:

- Publishing in the area of CFS.
- Being familiar with the latest research on the etiology of CFS.
- Being familiar with the latest research on diagnostic markers.

We found that over two years, only about 15 percent of study section members worked on anything related to CFS. There were no experts in etiology and maybe one in cytokines and the immune aspect of CFS.

The word is out that this issue exists with this study section. If I'm a young person with a good idea, I'm going to think carefully before I submit that proposal because I'm not sure if it's going to be worth the work. If I'm a senior person, it depends on the status of my laboratory and whether I have the resources. It's an issue that I hope would be addressed as NIH institutes its policy of multidisciplinary research.

I testified on a panel before Congress several years ago on the NIH budget. We were asked whether an influx of money would promote interdisciplinary research. We responded that money wouldn't make much of a difference without a change in the review process. If you have the same study sections with people who don't have the background in the appropriate area for the grant coming through, that grant's not going to get funded no matter how much money is there. The whole field doesn't move forward, not because there's no money, but because of the nature of the study sections.

Dr. Hanna: The person coming to testify from CSR should have some answers if there are any answers. I wish you had looked at the review panel for RFA. People complained about that panel too, and you see what kind of research we funded.

Mr. Newfield: Is it within this committee's purview to make a recommendation for or influence in any fashion the composition of a study section?

Dr. Parekh: My advice is to listen to what Dr. Kitt [from CSR] has to say, and then there will be ample time for discussion. The purpose of inviting her was to get to this.

Dr. Glaser: The change coming at NIH provides a great opportunity not to point the finger and criticize, but to take advantage in a positive, constructive way so that when those new panels are eventually established, they have people who know CFS and make the PIs feel that their grants are going to get reviewed by people who have some expertise.

Dr. Klimas: At the CDC you work through both contracts and collaborations. Is there any way that we can get some feedback on what work is going on through CDC's contracts and collaborations?

Dr. Reeves: The money that CDC allocates to CFS goes to contracts and cooperative agreements. We do not do grants. Everything we do has to fit into the research strategy of trying to control the illness. As far as exact amounts of money spent, I can tell you what I have in my program records, but that is not necessarily everything that CDC has spent. Public awareness spending is money that goes toward CFS, but it is funded through the Office of the Director. There is overhead and other salaries that are supporting this. To get the officials amount, it must come from the Financial Management Office.

Dr. Klimas: You're showing us your in-house spending. What's going on outside of your house that you're encompassing in your program?

Dr. Reeves: Right now, nothing…other than the series of Cold Spring Harbor workshops. They are trying to help us answer questions and at the same time they're trying to get people together so that they can answer their own questions.

Ms. Artman, Chair of the Quality of Life Subcommittee reported:

- **Our primary focus is third party payers.** We sent out a letter inviting several medical and long-term disability providers including Aetna, Cigna, Humana, BlueCross BlueShield (BCBS), Nationwide Health Plan, and Kaiser Permanente. Of those, we received a written response from BCBS, and CMS will be reporting to us tomorrow.

  We want to know what is and isn't covered for patients and the insurance companies' justifications for what they cover when they're trying to get someone to return to work. This has a huge impact on patients' lives. If you are unable to work and you need treatment and then you get to the point that you might be able to return to work, what are the detriments in getting you to the point that you can actually go back? How much do the insurance providers want to invest in you as a person to help you return to work?

- **We are greatly interested in the CDC's Georgia study.** We're concerned that there is not enough money to complete a longitudinal study. We think it would produce relevant quality of life information beyond what's going on now to show how patients react to a long-term illness, specifically CFS.

- **We discussed the need for patient education**, since the Education Subcommittee's emphasis is on physicians. We've come to realize that there's also a problem with patients not knowing their illness. Sometimes they don't go to the doctor for a symptom because they think it's "just CFS". Dry skin, for example, might not trigger a trip to the doctor when brain fog is your big issue, and as a result, your hypothyroidism might not be diagnosed. Patients need an education so that they can be responsible for their own healthcare. All burdens for this illness should not be put on a provider. Patients need the tools to manage their own lives and take care of their own health.

- **We are eager to have ARHQ here today** and we want them on our subcommittee. We think that they have a lot to offer to quality of life.

- **An on and off issue has been the name "CFS", which has caused so much controversy within the patient community, as have multiple case definitions.** We have discussed whether there needs to be another DHHS panel to come up with another case definition. We don't know if it's necessary at this time, but we think that it's something that we should at least consider. Changing the name of CFS isn't going

- **What we really need is to find is the biomarker.** Once we have a biomarker, we can go a million other places that will legitimize the illness and do great things. We would like to encourage the NIH in any way, shape, or form to nurture research into finding a biomarker. We applaud NIH for its efforts in this direction.

Mr. Newfield continued the subcommittee report

We spent some time really trying to access the third party payer community. We were all skeptical about whether they would step up and actually interact, and we were largely right, other than one response that we received from BCBS. Those answers bring up further questions and concerns. Our hope is that we might be able to influence and/or access some additional information from CMS that might shed light on some of these issues. If CMS takes certain positions on coverage issues, the insurance companies might be more inclined or compelled to follow suit.

One of our areas of concern is the level of training and qualifications for insurance company employees who review CFS cases to determine eligibility for treatment and services. BCBS replied that initial determinations are made by "trained and experienced nurses". We know that there is an absence of even doctors in this country who thoroughly understand CFS issues. These nurses are reviewing records and making determinations that potentially conflict with treating physicians who are experts in this field.

"Adverse determinations"—which are appeals of initial determinations sent back for insurance company review—are supposedly being reviewed by appropriately trained and experienced physicians. Who are these physicians reviewing these claims? My experience is that these are non-practicing physicians. Even assuming that they are practicing physicians, they are probably not practicing in the CFS field and certainly wouldn't be on par with specialists. They are making claim determinations based on a paper record. It raises the question whether CFSAC can influence these insurance companies to provide further (real) training for doctors who are making CFS claim determinations.

I have seen through direct experience how disability claims are evaluated through paper reviews by non-qualified physicians. There are probably many more health insurance claims than there are disability claims. This situation carries over to the issue of guidelines. CMS may be able to institute some sort of guidelines that might filter down and influence the insurance companies.

We posed other questions to the insurance companies, such as whether there is an age below which a diagnosis of CFS is not accepted and how coverage is handled for off-label or off-indication drugs that could be helpful.

We are pleased that the Education Subcommittee identified AHRQ as a potential *ex officio* member. That's certainly on our radar and we want to take the opportunity to consider it

following ARHQ's presentation. Next, Chris [Snell] has an angle on provider and patient education that is an important and often overlooked consideration.

Dr. Snell: I think everyone who deals with CFS patients is aware of the importance of a family support network, particularly to quality of life. We see a future when family care givers are becoming more important in providing health care and home support for people who are sick. This seems to have been going on for a long time for CFS. We should be encouraging the development of a support network and education along the lines of a toolkit for family health care providers. That might be something that we could promote.

Dr. Oleske: I would second the notion of quizzing AHRQ and CMS carefully, especially in regard to what is and isn't covered. I was disappointed by the lack of response by third party payers, but it will be interesting to see if we can get CMS to be more involved in CFS. What they say will be picked up by the third party players.

I wanted to bring up something about education. Wikipedia is popular with my medical students. I would say that for half the medical students, their initial search is done through Wikipedia. We may criticize it or not, but it's a reality. It may be an educational tool that we can use. Maybe we should have the Education Subcommittee look at Wikipedia and make sure that it's accurate.

Dr. Jason: We're currently involved in doing that. We'll have a report on that at the next CFSAC meeting.

Mr. Newfield: We have encouraged the full committee to throw out ideas with respect to CMS. We would like to hear particularly from the clinicians on what we would like to accomplish with CMS.

Dr. Reeves: Is there any evidence that BCBS is worse at reviewing CFS claims than it is for any other client? If they're pretty mediocre at everything, then you're really dealing with the entire issue of training.

Mr. Newfield: My view when I deal with insurance companies is that they tend to be for-profit entities. Their goal is to minimize the amount of payments that they make.

Dr. Reeves: We're dealing with adjudicators and reviewers. Also, we will be talking about your suggestion about education for home care givers at our next meeting. That is not an issue that I've thought a lot about.

Mr. Newfield: The insurance industry has outside doctors who pander to them. I was at an insurance industry conference where a presentation was made by a doctor who characterized CFS and fibromyalgia (FM) claims as being "all in their heads". It emboldens these claims people, who are the front-line decision makers for the company, if this attitude has not already filtered down to them from higher up. There are also potential bonuses for denying legitimate claims.

With regard to the issue of further training, I want reviewers to have information and be educated on CFS; then let them try to ignore it. I have tough standards as an attorney in proving these cases. It may help if I can point to the fact that insurance officials were given all of this good information that allows them to appreciate the significance of this illness and then choose to ignore it.

Dr. Oleske: This is a legitimate area in which this committee needs to be involved. As a person who sees adolescents with CFS, I spend the majority of my time explaining to the parents that their adolescent is sick; that you don't need to smack them on the side of the head and tell them to go to school as a way to treat this syndrome in their children. I hope we can include family education, because with adolescents with this disease, the fathers are frequently very hostile towards the kids with CFS. The mothers are usually more in tune with what's going on with the child. We do need to reach out to families, because they have a desperately poor education on what's going on.

And the school systems—I can't tell you how many hours I have to spend and letters I have to write to some school systems justifying the need for two sets of books. Yet that basic simple premise is lost on some school systems. They fight tooth and nail against home tutoring and they will fail kids.

Dr. Parekh: Jason, based on your experience—there's probably no data on this—what are the types of claims from CFS patients that are rejected by insurance companies?

Mr. Newfield: I don't do a lot of work on the healthcare side with respect to individual medical coverage. For disability claims, clearly, they choose to rest upon a lack of objective evidence. If you had a test for CFS and you could identify it in some meaningful way, you would overcome that burden that they've imposed. They ask for objective evidence even when the contract doesn't require it. Some judges note that without such evidence, they would have to rely on what the claimant says. But there are a lot of cases in which self-reported subjective complaints can establish disability. We have a spectrum of judges that view the same set of facts differently.

When surveillance is conducted of a patient and it is during the time that he or she goes to the mailbox or drives to pick up medicine, that gets extrapolated into being inconsistent with what the patient reports. Or insurers love to send patients for what is called functional capacity testing. If you, the patient, push through the test, it never gets revealed that you spend the next several days in bed because you pushed beyond your physical capabilities. It gets extrapolated that you have a full 40-hour work week functionality based on three hours of testing. Or, worse yet, you limit yourself because you know you can't keep pushing, and they say you have self-limiting behavior and suddenly you're a malingerer. You're damned if you do and damned if you don't under such testing even though the contract may not require it.

Dr. Parekh: Rebecca, what do you hear anecdotally from the CFS patient population about what claims are denied?

Ms. Artman: What I have heard anecdotally is that you never want CFS as your primary diagnosis. You want to have anything else as your primary, and CFS as your secondary. My insurance provider, which routinely covers acupuncture for other illnesses, said that it's not covered under the conditions that I have as my diagnostic marker. When I renew my contract every year, I notice that there are more and more exclusions. I've also noticed that every year my copay increases and what's actually covered is decreasing. My monthly rate right now is $455/month, which is a deal.

Dr. Klimas: I have patients that spend $900/month for their COBRA policies and that excludes CFS. This is why insurance company policies raise billing practice concerns for me and any physician treating CFS patients.

Ms. Artman: When I was first diagnosed and was seeing my family practitioner, who did not know the billing code game, everything was denied—every blood test. I paid for all of them with cash.

Dr. Oleske: The problem that I see as a clinician is that I've never before been asked for my boards in immunology to order tests. One of my nieces has CFS, and they filmed her going to her child's Chuckee Cheese birthday party. She spent a week sleeping and getting rested up for that, and they denied her claim saying that anybody who can take her kids to Chuckee Cheese for a birthday party can't have CFS.

Dr. Klimas: We have a real big problem. There seems to be no rational way to approach the problem as it is currently laid out in the common practice of medicine.

Dr. Oleske: It is the patients who pay a huge price.

[Dr. Oleske called a five-minute break]

Update – Peer Review Activities and Initiatives at the Center for Scientific Review

Dr. Cheryl Kitt, Deputy Director, *Center for Scientific Review, NIH*
Accompanying Document – *Enhancing Peer Review: NIH/CSR Challenges and Initiatives*

There is a move within CSR to enhance peer review and it affects every study section and all that we do. CSR receives every grant application that comes to NIH. We also review for the CDC, AHRQ, the Department of Defense, and anybody else who asks us to review.

- About 90 percent of the applications of the 80,000 we receive in a year are investigator initiated, not solicited by RFAs or RFPs. That doesn't mean that you can't move the field along. Program directors, patients, advocates, and lobbyists do that by talking to investigators about particular interests.

- About 60 percent of the applications CSR receives are basic research. Clinical research is still a challenge.
- 25 percent of the applications are from new investigators. There is a Congressional mandate that we increase funding for new investigators, so there is extra funding for them right now.
- CSR has three major deadlines a year.
- The time from application to funding is about nine months. There are some initiatives at NIH trying to truncate that time period.

2006 CSR Statistics

- 80,000 applications were received.
- CSR reviews 57,000; the rest are reviewed by the 22 NIH funding Institutes and Centers. Those are mainly the big projects, the program projects, the Center grants, the career awards, and the RFAs and contracts.
- CSR has 250 Scientific Review Administrators.
- We conduct about 1,800 review meetings per year using about 18,000 reviewers.

The number of applications that we receive per year began increasing in 2002. Historical growth up until that point was relatively flat, with a very slow increase. The jump beginning in 2002 does not necessarily track with an increase in investigators, who are submitting more applications per person. In the past, they submitted about 1.2 applications per investigator; now it's almost 1.5. That works out to about 10,000-12,000 more applications per year.

People who review grants are also grant applicants and busy researchers themselves, so they don't like to review a lot of applications. We try to accommodate that by giving them a lighter load but as a consequence, we use a lot of people. "Chartered" study section reviewers agree to come to NIH three times a year for four years. We have a steady number of committees (about 250) that are chartered by Congress. Each committee has 20 or so chartered members.

CSR needs ad hoc reviewers to keep up with the increasing need for expertise. These ad hoc reviewers may review just one application for one specific scientific area, or they can review many applications.

Study sections are organized into 23 Integrated Review Groups (IRGs), soon to be 24. The new group will be devoted to neuroscience, including technology and training. The IRGs report to five scientific divisions that represent five scientific domains.

CSR has many Special Emphasis Panels (SEPs). With only 250 standing committees and 1,800 review meetings per year, that means that about 1,300 of those meetings are SEPs. Congress mandated that we have an SEP for CFS. Other SEPs exist to accommodate the number of applications. If we receive more than 80 applications in an area, we must spin off a SEP. The panel's emphasis is usually on science, although it can be on the mechanism. [A mechanism is an R01, the "gold standard".] CSR has also seen a tremendous increase in R21s, which are frequently about feasibility, high risk, high impact preliminary studies. They

have increased dramatically over the last few years because in many people's minds, the R21 looks like a "mini R01". Researchers are taking advantage of R21's as another grant application route.

The criteria for selecting peer reviewers are rigorous:

- They include a requirement that the reviewer has grant funding and is conducting some type of supported research. For the most part CSR reviewers are academic researchers.
- CSR also reviews small business applications, so we have a community of small business owners/researchers who serve on review panels.
- Some panels include members of the public who have some background in science.
- Reviewers must meet internal administrative considerations, the most important of which is more stringent conflict of interest requirements, both scientifically and financially.
- Review panel membership has standards for diversity in geography, gender, and ethnicity.

CSR looks for broad expertise in its CFS SEP members, but if an application concerns a specific science, we will certainly put experts in that area on the panel as well. The CFS SEP tends to act like a standing committee because it meets repeatedly from year to year. We try to provide consistency of review, but no law or regulation requires that a revised application must go back to the people who reviewed it before. No statistics are kept about the success of revised applications that are reviewed by the same panel members as opposed to revised applications reviewed by a different group of people.

Much of the CSR email concerns complaints about NIH peer review:

- The process is too slow (nine months).
- Not enough senior experienced reviewers on committees. CSR takes this seriously. We limit the number of very junior people. If they're in a burgeoning new science, however, they may be the only experts in the area. We are establishing a national registry of potential reviewers. I urge CFSAC members to recommend reviewers who haven't served or who would like to serve again. We will report back to you whether we use them.
- The scientific community feels that the review process favors predictable research as opposed to innovative, transformative, risky research. That's probably true, but CSR is making an effort to address this issue.
- The process is burdensome for reviewers.

Current Initiatives for Solutions

Shortening the nine-month review cycle

The life blood for junior faculty is getting a grant. Under the CSR review cycle, it took up to two years to determine whether or not a grant is awarded, by which time these faculty members had no chance of tenure. As of November 1:

All new investigators can come in three times a year with an R01 application (one original application and two revisions. This also applies to senior investigators.

- New investigators receive summary statements within 10 days of the meeting—a minimum of two weeks, but frequently as much as one month before the next deadline.
- As of 2007, there are 12,000 new investigators eligible to take advantage of the streamlined review process. CSR will track how well they succeed. So far, about 13 percent of new investigators who were eligible to come in early did so. Twenty-five percent of those grantees were funded a year earlier than they would have submitted the next revised application under the old process.
- CSR is going to interview the successful applicants about the process.

Immediate assignment of applications to IRGs. We started a pilot using knowledge management tools (algorithms and logic) to do text mining of cover letters. About 50 percent of all investigators submit a cover letter with their application and we honor more than 90 percent of them just based on what the PI says because, frankly, the PI usually knows best where the application should be reviewed. Machine learning algorithms search for key words, then match where that kind of science would have been reviewed in the past. Eighty-two percent of automatic referrals agree with the final referral by experts, which is almost as accurate as human screeners. Automatic referral has cut 10 days from the process of human referral to study sections. CSR will implement automatic referral in February 2008.

Realigning of study sections.

- Internal reviews of all 23 IRGs used to occur every five years. That has been reduced to every two years. We look at the IRG's work load and what science is covered.
- We see fluctuations in numbers of applications in study sections and sometimes these persist and become recurrent SEPs. At that point, we consider creating a standing committee for that science. We created seven new panels in the last year.
- CSR will have conducted six open houses by the end of 2007 organized according to scientific clusters. These meetings are open to the public and are attended by the study section chairs, two members of the professional societies to which these scientific areas belong, the NIH community, and investigators. The open house workshop helps CSR answer:
    1. What will be the most important questions and/or enabling technologies forthcoming within the science of the discipline in the next 10 years?
    2. Is the science of the discipline, in its present state, appropriately evaluated within the current study section alignment?

  These workshops have consistently highlighted one concern: there does not appear to be a home in CSR for the review of multidisciplinary or transforming

science. That's something that we're going to follow up on. The results of these workshops are posted for public comment.

Electronic reviews: expanding peer review platforms.

CSR has had difficulty getting reviewers in any clinical or surgical specialty. Our goal is to have at least 10 percent of all reviews to be electronic in 2007 and it looks like we've exceeded the goal. This will not supplant face-to-face meetings. What we would like to do is have one electronic and two face-to-face reviews per year using:

- **Video and telephone-enhanced discussions with live cameras.** These have helped in scientific domains where we need experts from China, Africa, India, and the rest of Asia. We send video cameras to the reviewers and they can keep the equipment because it costs us too much to pay for their return.
- **Asynchronous electronic discussions** (AED) similar to web chats. Reviewers can type in their comments anytime within a three-day window of the meeting. The discussions are very rich, perhaps because the reviewer is less self-conscious about being honest than he or she would be face to face. AED brings in very senior people who would not ordinarily be available for review.

Shortening the size of the applications.

- At 25 pages, R01 applications are the biggest research plans in the world.
- An NIH survey on shorter R01 applications showed that 73 percent of reviewers and applicants prefer an application that is 15 or fewer pages.
- The Trans-NIH Short Application Design team is discussing what gets left out or shortened and is calling for public comment. One idea is cutting out the methods section based on the reasoning that if the project is not a good idea, why spend time reading about methods? Why not list the URLs? Why not have only one page for significance? If the reviewer has to comb the application for significance, the applicant is already in trouble.
- The redesign will include the review criteria and critiques so that they are in concert with one another.
- A shorter application can mean that reviewers focus more on impact and innovation and less on method and preliminary results.

Abolishing submission deadlines.

This proposal was originally for researchers who are permanent members of study sections and is scheduled for possible implementation in February 2008, but there is strong support for applying it to everyone.

Editorial Board Reviews for complex, multidisciplinary, and translational research. The advantages of this format would be:

- Emphasizing significance and impact.

- Providing specific expertise in a wide range of scientific areas.
- Making efficient use of reviewers' time by answering quickly whether the question is valid and important.

Online: http://enhancing-peer-review.nih.gov/
Email: kittc@csr.nih.gov

Committee Members Q&A

Dr. Glaser related his experience of attending the CSR Behavioral and Social Sciences Open House Workshop. Behavioral sciences tend to be multidisciplinary, and there was a consensus among those attending that the MESH [Biobehavioral Mechanisms of Emotion, Stress, and Health] study sections are working. The same does not apply in CFS study sections. Over the last three years, only about 15% included members who work on CFS, and none of those people worked on the etiology. **Dr. Kitt** responded that very few people have CFS as their primary research area and that CSR has tried to recruit them all. They have not been able to serve because of time or conflict. Dr. Glaser concluded that NIH owes it to the PIs in CFS research to give them the fairest review that they can get, and Dr. Kitt agreed.

Dr. Klimas: There's a strong feeling among investigators that getting a review by the same set of reviewers the second time could substantially improve your chances of funding. This can be done in a way that keeps the identities of the reviewers confidential.

Dr. Kitt: Based on anecdote and experience, when an investigator requests that we send it back to the same reviewers, we try to do so if we can. When we do, the success rate often doesn't change. The same problems are not being addressed in the application. Just sending it back to the same people may not be the fix that you're looking for. It is unpredictable even with the same reviewers. Every reviewer should read all of the applications, but it doesn't always happen.

Dr. Glaser: IACFS has sent in large lists of potential reviewers for four or five years. We have tried actively to present issues and potential reviewers. We want to continue this dialog. Also, you might consider whether membership on CFSAC should count as a conflict of interest for CSR review.

Dr. Kitt: Anyone who serves on a federal advisory committee is recused from reviewing anything in that scientific domain. CFS is a small area and there are a lot of conflicts.

Dr. David Atkins, Chief Medical Officer, *Center for Outcomes and Evidence, AHRQ*
Accompanying Document: *Defining and Managing Chronic Fatigue Syndrome*
Summary (www.ahrq.gov/clinic/epcsums/cfssum.htm)

AHRQ Mission: to improve the quality, safety, effectiveness, and efficiency of healthcare.
ARHQ Budget: $300 million/year, which is one percent of the NIH budget. A lot of ARHQ's

budget is pre-allocated to specific activities. The amount we have for investigator-initiated research is a recurring problem.

AHRQ research: traditionally related to health services, so we're not involved in discovery of new treatments. We're focused on:

- Accelerating how quickly effective care gets picked up in practice.
- Related issues of clinical practice, healthcare design, policy, and reimbursement.

Current areas of emphasis:

- **Patient safety** for both in-patient and out-patient care. Medical errors have gotten the attention, but patient safety encompasses more than just preventing errors.

- **Health information technology**. Many recent grants have been in this category.

- **Comparative effectiveness**. AHRQ has recently received Congressional funding in this area. We compare treatments for conditions—not just pharmaceuticals, but also surgical, behavioral, and technology-based treatments. Our research enterprise has been good at evaluating individual therapies, but at not comparing therapies or assembling the evidence to help a patient, clinician, or health system decide which choice is best for a patient and what factors go into that decision.

- **Support of several large research databases:**

  Cost of care – a medical expenditure panel survey that is good for evaluating costs of individual conditions but is limited by sample size. Useful for looking at national costs for common conditions; not adequately powered to look at CFS.
  National database of hospital discharge data – the HCUP [Healthcare Cost and Utilization Project] survey includes data on trends and uses, and factors related to outcomes in hospital-based, emergency room, and ambulatory surgical care. **Several large clearinghouses** that include the National Guideline Clearing House, an international set of more than 1,000 evidence-based guidelines on a wide range of conditions. AHRQ also has a National Quality Measures Clearinghouse and the Innovations Clearinghouse of innovations in healthcare.

- **Support of several research networks** useful for studying specific questions:

  Primary care practice-based research network that includes more than 15 conglomerations of practice-based care. Good for studying translation and doing new research that has a primary care focus.
  A complementary research network called Action whose members are integrated delivery systems. Useful for determining whether something can be taken to scale in large healthcare systems.
  Evidence-Based Practice Center Program, a network of 14 evidence-based practice centers that do research syntheses. In 2001-02 we did a synthesis on CFS treatments

and another report looking at measures and evidence of disability. In the program's early stages, we had difficulty evaluating research that didn't fit the standard clinical trial model. We now are interested in synthesizing a wider array of research, including observational research.

AHRQ Effective Healthcare Program

1. Ability to synthesize the evidence, which we do through our evidence-based practice centers. These centers are meant to generate new information often directed at gaps in knowledge that are identified by our research syntheses.

2. Ability to access large data bases, both administrative and clinical, at our research centers. These data bases include both in- and out-patient data covering more than 50 million people, the largest collection of observational data. Their limitation is that the data may not be rich enough to examine the kinds of issues that require discrete clinical data.

3. Ability to translate research information for patients, practitioners, and policymakers at the AHRQ translation center.

All three efforts are designed to be transparent and we accept proposals from a variety of stakeholders. We have an aim of addressing things that are a high priority for federal healthcare payers such as Medicare and Medicaid.

Committee Members Q&A

Dr. Klimas asked **Dr. Atkins** whether he would be interesting in working with CFSAC. Dr. Atkins responded that he is not completely familiar with the CFSAC mandate and mission, but noted that AHRQ can contribute most where effective care has been reasonably well defined and but is not being taken up in practice. If the issue is the need for more research on effective interventions and understanding etiology and prognosis, AHRQ does not have as much to offer.

Dr. Klimas responded that AHRQ could be useful in two areas:

1. Getting people with chronic and disabling fatigue to their clinicians and having those clinicians be confident enough to treat the conditions.
2. Developing clinical guidelines that could be implemented.

Dr. Oleske agreed, pointing out that a lot of Americans suffer with CFS. While there is no diagnostic test, there are treatments that need more vigorous guideline development. Many CFS patients also have symptoms that could be treated, but aren't. While people feel that it's hard to develop guidelines without a diagnostic test, that all too often makes for orphan diseases, and CFS should be mainstreamed. AHRQ would be an ideal candidate to be more active on CFSAC, he concluded, and there are many areas where patients with CFS could benefit from AHRQ involvement.

Mr. Newfield asked for more details on measures of disability and what that constitutes.

Dr. Atkins: We've done several reports for the Social Security Administration (SSA) to help them determine whether they can apply evidence-based methods to assess and quantify disability and to assist them in choosing the best tests. We learned is that it's a challenging process because the types of evidence are not the same as those in a typical hypothesis-testing trial. I'm not sure that these findings were a help in clearing up the current debate about the best ways to assess disability.

Dr. Jason: Who would be the contact person for someone who wanted to talk to an AHRQ program officer about CFS/ME? Would you be willing to talk about possible projects within AHRQ that scientists might be able to propose?

Dr. Atkins: I could be at least the short-term contact. AHRQ's perspective may be useful to CFSAC because it has links to the healthcare systems and primary care. In terms of research proposals, I would have to say that an R01 proposal coming to us in the current funding environment might be tough, but if it fits with our broader areas of emphasis, it might be possible to take ideas to our research network.

For example, if the proposal addresses the problem of diagnosing CFS at the first point of contact in primary care, our practice-based research networks would be a way to study that. The primary care angle is a good fit. ARHQ would find it of interest to know more about the initial care points of contact, the skill set necessary among primary care clinicians, and the barriers that CFS patients face in getting the right initial evaluation and diagnosis. There are issues there on which we could potentially collaborate. I can put you in touch with the people who are in charge of that area in our Center for Primary Care and Clinical Practices.

Public Comment

Annette Bacola, Advocate for Ampligen availability

I showed signs of severe skin allergies for the first time after a serious viral infection in my mid-twenties. Heavy doses of steroids, tranquilizers, and other drugs artificially kept the allergies at bay but forced me to give up a television anchoring position.

The next few years brought more allergies to many substances, including chemical perfumes and smoke, and insidious symptoms such as bouts of fatigue, frequent muscle aches, and weaknesses. A variety of doctors from dermatologists to chiropractors prescribed numerous treatments, including antibiotics and antihistamines. Meanwhile, I used all my energy for my demanding business career and took the weekends to lie in bed and recuperate, even as my decreasing energy level restricted me to doing less and less.

I finally found enlightened MDs who knew about CFS, Candida, and multiple chemical allergies. One such physician, an allergist, put me on antifungal medication, a strict diet, and

carefully chosen nutritional supplements. I attribute that treatment for enabling me to get pregnant and enjoy a healthy pregnancy.

I crashed after giving birth, however. I also moved to Chicago, lost touch with my New York physicians, and ended up unable to work full time for another three years. Eventually, although my health was not good, my illness became predictable enough to take a political position running a state agency in Michigan. With great effort and coping techniques that would be familiar to any CFS patient, I sustained the job for four years. It eventually became too much of a struggle, and I resigned with two years left on my second term of office.

By this time, I was allergic to almost everything and suffered severe bouts of fatigue and neurological symptoms such as disorientation and cognitive difficulties. I had no ability to regulate body temperature and felt like I was freezing all of the time, but I also could not tolerate overly hot weather. As a last resort, I went to the Mayo Clinic in Minnesota. Their diagnosis was CFS and multiple chemical sensitivity—depressing, but at least a tangible diagnosis. I struggled to maintain a health lifestyle, keep exercising, and take supplements that work for me. The only way that I've been able to work is at my own pace. Anything that creates physical or mental stress can trigger me to crash. I continued to see both conventional and alternative practitioners.

In December 2005, I saw a website featuring Dr. Lucinda Bateman and her practice involving CFS. I called to make an appointment, but was told that she had a year-long waiting list. I did have a conversation about a clinical trial that they were conducting on Ampligen. After researching the drug and with the support of my husband and then nine year old son, I temporarily relocated from Kentucky to Salt Lake City to participate in the trial.

I noticed a difference with Ampligen almost right away. I perceived feeling stronger with more energy after the treatments. The study indicated a gradual increase in dosage until the prescribed dosage is reached, and I started having side effects—dizziness, disorientation, and ocular migraine spells 90 minutes after the drug infusion. These subsided within an hour. At Dr. Bateman's suggestion, I started taking a half-dose of an over the counter migraine medicine right after the treatment, and the all the negative symptoms stopped.

My health in the next few months was the best it had been in years. I was admittedly overdoing it, traveling and not getting enough sleep. I still had the allergies and chemical sensitivities, but the lows were not as low and the highs were much higher and more frequent. I was functioning at about 90 percent of normal, and as a driven, energetic person, my version of normal has very high standards. I left Utah to return to my family and attempted a twice-weekly commute to Charlotte, NC, to stay in the trial. The commute was difficult from my home in Kentucky and I reluctantly went on a drug holiday. That was almost a year ago. Although my health now is better than it was before getting Ampligen, I'm not close to functioning at the level I achieved with Ampligen.

I'm optimistic that one day this medication will be readily available to CFS patients and others who need it. I know it to be a powerful medication capable of addressing a life-long illness.

Who knows how many viruses are out there that will present themselves in the next few years that could be fought with this drug?

Cort Johnson, Founder/Publisher, *Phoenix Rising* website and newsletter

In 2001, NIH was still funding three cooperative research centers that, at their peak, were funding 43 grants and publishing 10-15 studies per year focusing on CFS. NIH is currently funding 14 studies on CFS. Except for the small bounce given by the neuroimmune RFA, NIH has only been able to fund 1-3 new studies per year over the past five years: two in 2003, one in 2004, one in 2005 and three in 2007. Of these, almost half are short-term, two-year studies. This for a disease believed to affect more than four million Americans and cost $20-25 billion a year in economic losses.

The ORWH's neuroimmune RFA was a disappointment, with only a quarter of its projected funds going directly to CFS research. The NIH projects that CFS research funding from 2003-2008 will decline by 50 percent, from an embarrassingly low $6 million to $4 million. A search of long-term funding levels for more that 200 diseases and conditions indicated that no other program has had its research funding decline so dramatically.

Dr. Hanna has said that difficult budgetary times are hampering research everywhere. She has said that neither new RFA grant packages nor Centers of Excellence programs will be forthcoming for CFS in the near future. Yet a major RFA grant on pain was recently announced, as was a Centers of Excellence program on cancer. It's clear that the current budgetary problems at NIH have little to do with the long-term decline of the CFS program. Even when NIH budgets were at historical highs, the CFS research program was floundering. During this time, the CFS Working Group (CFSWG) failed to endorse a Centers of Excellence program, dragged its feet on producing a small RFA grant, and then failed to act proactively to ensure the grant's success.

We have a conundrum. How does it happen that these knowledgeable and concerned people have presided over the worst decline in any CFS research funding in its history? Why are one or two or three grants funded a year in a disease that affects millions? When such events happen on the watch of good and concerned people, it's evident that they face major roadblocks. These roadblocks do not originate at the ORWH. I suggest that the CFSAC needs to find out where these roadblocks are. I request that the committee invite CFSWG representatives to a meeting and ask the following questions:

1. How is CFS perceived at their particular Institute?
2. What issues do they face in building a strong CFS research program?
3. What kinds of negative perceptions do they need to surmount?
4. Why was NIH able to fund three cooperative research centers and an extramural grants program but is unable to do so now? What has changed?
5. Given the dramatic decline in CFS research funding over the last five years, why is a Center of Excellence or research center program not a viable solution?
6. What can CFSAC do to aid CFSWG members in their efforts to build extramural

programs?
7. What are the projections for CFS research funding over the next 5-10 years?

Mary M. Schweitzer, PhD, Advocate for availability of Ampligen
Accompanying Document: ***Testimony before the Chronic Fatigue Syndrome Coordinating Committee (CFSCC) of the U.S. Department of Health and Human Services***

Dr. Schweitzer distributed copies of testimony that she gave in 1999 to CFSAC's predecessor because "nothing has changed. Everything that's in there is just the same.

I was a tenured professor of history with an active research program. My husband is also a professor. We have two children, we skied, we traveled, and everything was going great until October 24, 1994, when I turned into a zombie. I was grading papers in my office and suddenly I could not read or understand anything that was on the papers.

By the fall of 1998, I had diagnosed problems with fluid balance, thyroid, temperature regulation, natural killer cell function, sleep, emotional ability, sequencing, abstract reasoning, memory, expressive dysphasia, and constant pain behind my eyes and the back of my neck such that on some days all that I could do was lay in the dark listening to my favorite movies. Loud noises and bright lights were painful. I had difficulty understanding what was spoken to me, sometimes I had double vision, sometimes I had tunnel vision. I understood little of what I tried to read, and I had difficulty with distance, spatial, and depth of field perception.

On February 4, 1999, I began treatment with Ampligen at a point where I could barely stand long enough to testify before CFSAC. I turned in my wheelchair in April and began driving again in May. I read a novel in August and danced in my son's wedding in September. At that point, Ampligen cost me $40,000 a year. My entire family was contributing to this. I went off it after 20 months because it seemed the right thing to do. One year later, I collapsed again. It took seven months to get back on the drug because it wasn't FDA approved.

Patients who participated in the six-month Ampligen study got six months worth of the drug, then relapsed. I would like to see Ampligen at the level where it is tested at universities and tested for its interaction with other drugs. If I lose access to it, I will go back and I will go back quickly, and that's terrifying to know. I would like to see this drug fast-tracked. We do not understand why it hasn't been fast-tracked because it meets the requirements.

I have markers. When I had the markers, I was sick. When I didn't have the markers, I was well. A famous economist once said that the singular for data is anecdote. You can't say that there's nobody who ever improved on this drug because I'm here to tell you that I did. Please, dear God, do not take it away from me again.

Nancy McGrory Richardson, Education and Outreach Coordinator, ***Hemispherx (the company that developed Ampligen)***

Accompanying Document: ***Email from CFS patient Anita K. Patton supporting***

availability of Ampligen

Ms. McGrory explained that she has a health science risk assessment background and has done work in chemical and environmental exposures, post traumatic stress disorder, and multiple chemical sensitivity, among other areas. She read the letter of CFS patient Anita K. Patton describing her positive experience on Ampligen and advocating its availability to all CFS patients.

Dr. Snell: It would really help the scientific community if Hemispherx published the study for its double blind trial. At the moment the science is only anecdotal and we can't put the full force of this committee behind anecdotal evidence.

Marly Silverman, Founder, *P.A.N.D.O.R.A.*
Accompanying Documents: *Presentation to the CFS Advisory Committee (CFSAC)*
November 29, 2007
CFS Patients in the United State Share Their Stories

We believe that it is time for this committee to push for fast-track approval by FDA of a drug specifically for CFS/ME. Our board has contacted large and small pharmaceutical companies and has received feedback that contains some common denominators:

- A perceived lack of interest and/or involvement by NIH, CDC, and/or FDA; lack of a clear-cut initiative from a government agency to address CFS.
- Challenges faced in coping with the complexities and variability of CFS.
- Too many financial restraints and not enough earnings potential.

I would like to ask CFSAC approve a recommendation that would stimulate and jump start the interest of pharmaceutical companies in the United States and abroad.

Ms. Silverman also presented other items and news to CFSAC:

- Pictures and personal letters from CFS-ME patients and their caregivers who are part of the EMPTY CHAIR PROJECT. They could not attend the CFSAC meeting because of health or financial limitations. P.A.N.D.O.R.A. asked on their behalf that CFSAC provide real-time access to meetings via live feedback.

- Dr. John Rock, dean of Florida International University's College of Medicine, has partnered in principle to create a Florida Neuroendocrineimmune Institute for a possible opening in 2010-2011.

- In conjunction with the I NEED A HERO PROJECT, P.A.N.D.O.R.A. will shortly announce the creation of a medical scholarship to encourage medical students to choose the fields of rheumatology, immunology, neurology, or a closely-related field. A moral clause requirement of the scholarship would require the recipient to treat patients with FM and CFS/ME in his or her future practice or conduct research for these illnesses.

- P.A.N.D.O.R.A. will sponsor its first golf tournament on May 16, 2008 as part of its awareness month.

Adjournment

Thursday, November 29, 2007

Call to Order/Opening Remarks

Dr. Oleske called the meeting to order and congratulated invited speakers, community presenters, and the CFSAC subcommittee for providing material for honest and productive discussions. He reinforced the committee's desire to remain in contact with Dr. Atkins and involve AHRQ with CFSAC activities.

Roll Call/Housekeeping

Dr. Parekh took roll call, noting that Drs. Hartz and Desi were absent and that Dr. Hanna would be arriving later.

Dr. Parekh called for edits to the May 2007 meeting minutes. Committee members passed the minutes as edited.

Dr. Jyme Schafer, *Office of Clinical Standards and Quality, Coverage and Analysis, Centers for Medicare and Medicaid Services*

Medicare is a Federal health insurance program created in 1965 for all people age 65 and older and expanded in 1972 to include those under 65 with permanent disabilities:

- Those under 65 on Social Security Disability Insurance (SSDI) generally become eligible after two years.
- Exceptions are made for people with end stage renal disease (ESRD) and Lou Gehrig's disease. These people are eligible immediately upon receiving SSDI.

Medicare Overview

- Covers 43 million beneficiaries.
- 36 percent have three or more chronic conditions.
- 47 percent have incomes below 200 percent of poverty.
- 7 million in 2006 under age 65 were permanently disabled.
- Estimated cost in 2006 was $374 billion or 14 percent of the Federal budget.
- Provides no dental, vision, or long-term care (nursing home) benefits
- Private insurance plans are playing a larger role through the managed care program. They operate under different rules than the fee-for-service.
- Most beneficiaries of the Medicare program have some form of supplemental coverage such as an employer-sponsored plan or AARP.
- Very low-income beneficiaries are "dually eligible" for Medicare and Medicaid. This helps with premium and cost-sharing requirements.

Medicare has four parts that are funded differently and that have different rules.

Part A

- Pays for inpatient hospital, skilled nursing facility, home health, and hospice.
- It is funded mainly by a tax paid by employers and workers.

Part B

- Pays for physician, outpatient, home health visits, and preventive services.
- Funded by taxpayers through general revenues and beneficiary premiums.

Part C (Medicare Advantage)

- Private managed care plan such as an HMO, PPO, or private fee-for-service.
- Plans must offer Parts A and B coverage and many times also offer Part D.

Part D

- Created by Congress in 2003
- Outpatient drug benefit administered through private plans that contract with Medicare.
- Funded by general revenues, beneficiary premiums, and state payments.

Medicaid Overview

- Provides health and long-term care assistance for certain individuals with low income under Title XIX of the Social Security Act.
- State administered program enacted in 1965 as a partnership between the Federal government and the 50 states; Washington, DC; and the five territories.
- Largest source of medical and health related funding for the nation's poorest citizens.
- Federal statutes, regulations, and policies establish broad national guidelines that state and territory programs must follow.
- Each state administers its own program and establishes eligibility standards; amount, duration, and scope of services; and rate of payment for services. Since states administer their own programs, each is different. States design their own payment methods as long as they meet federal guidelines and can deliver services as fee-for-service, managed care, or waivers.

Medicaid must cover the following services: Inpatient/outpatient hospital, family planning, Rural Health Clinic/Federally Qualified Health Center, EPSDT for children under 21, nursing facility and nurse midwife, home health, nursing home, laboratory/x-ray, certified pediatric and family nurse practitioner, physician, medical and surgical dental, pregnancy-related.

Dr. Schafer listed 20 **optional Medicaid services** including occupational and physical therapy, dental, screening, preventive, and rehab services and prescribed drugs.

Medicare National Coverage Determination

Should we pay for the service? = coverage (Dr. Schafer's group)

Did we pay for the correct service correctly? = payment
Was the service we paid for performed optimally? = quality

In order for patient to get reimbursed he/she must have:

- Regulatory approval if applicable (FDA approval of drugs/devices)
- Benefit category determination (set by Congress)
- Coverage (set by CMS/CAG)
- Coding (CMS/CMM)
- Provision for payment

Congress determines the services that CMS can cover—they must be "reasonable and necessary" for the diagnosis and treatment of illness or injury or to improve function of a malformed body member. This does not include preventative services. Most coverage (90 percent) is local and is provided by contractors.

Local contractors are delegated the authority to process claims and have structured rules that they must follow according to the Program Integrity Manual. Medicare used to have 50 local contractors. Under the Medicaid and Medicare Act of 2003, contractors are being reduced to a maximum of 15. Local coverage determinations are made regionally.

Medicare National Coverage Process (Dr. Schafer's office)

When we get a formal national coverage request:

- We conduct an internal technology assessment, which is an extensive review of the literature. We can request input from a Medicare Coverage Advisory Committee or an External Technology Assessment from ARHQ, after which we conduct a staff review.
- We open two public comment processes—one when the determination is opened and one when the draft decision memorandum is posted.
- We release a Final Decision Memorandum and Implementation Instructions.
- The decision can be contested at the Department of Appeals Board. If new evidence emerges, the determination can be reconsidered.

A National Coverage Determination (NCD) is prompted most often by an external request due to substantial variations in local coverage or a move to get something covered that is not currently covered. Internally generated requests are rare. They are triggered by important new studies, technological advances with potential major clinical or economic impact, or concerns about inappropriate use.

CMS makes a determination of "reasonable and necessary" if the evidence presented is adequate to conclude that the item or service:

Improves net health outcomes based on the principles of evidence-based medicine (EBM). Lower quality studies and deductions from basic biology and pathophysiology are unreliable and treatments based on them could cause harm—or at least be ineffective. CMS

wants to focus spending on treatments that work. When judging the quality of evidence, CMS favors meta-analysis of individual patient data and large, multi-center random controlled trials over smaller studies and case-series reports.

Can be used generally by the Medicare population and provider community. Frequently we find that most of the evidence does not apply to people over 65 or does not include those who are disabled or with multiple co-morbidities.

Three decision outcomes are possible in an NCD: national coverage, national noncoverage, or national coverage with restrictions encompassing specific populations/providers or evidence development. The latter means that coverage hinges on prospective data collection and adequate evidence of benefit demonstrated in an appropriate study. The objectives of a decision in favor of "coverage with evidence development" are to:

- Promote innovation while obtaining value in healthcare.
- Speed access to promising new technologies and services.
- Improve available evidence.
- Better target treatments to the subpopulations that would most benefit.

CMS website with more details: www.cms.hhs.gov
Email: Jyme.Schafer@cms.hhs.gov

Committee Member Q&A

Dr. Oleske: Most CFS-related drugs will never be studied so the evidence base is always going to be weak. How do I make sure that children have access to appropriate drugs?

Dr. Schafer: That question is best addressed to NIH or FDA, not CMS. Coverage of drugs is Part D, so that's external.

Dr. Klimas: Are local providers allowed to exclude groups such as anybody with CFS?

Dr. Schafer: Local providers have to follow our national guidelines. Once you are a beneficiary, local providers cannot change that status. All people over age 65 are eligible for Medicare. The disabled under 65 who fit the criteria are those who have been on SSDI for two years. As to whether those eligible for Medicare can ever be excluded from being treated for the disease that disabled them, that's a legal question, and private contractors are making the actual determinations.

Mr. Newfield: What role does CMS have in influencing those entities to provide that coverage? Do you have that role?

Dr. Schafer: Congress tells us what to do. We work by mandate. If you fall into one of the criteria, you're covered. If we have a national coverage policy that Service X is covered, everybody must cover that. If we don't have a national policy, it's deferred to the local contractor. If the local contractor covers it, then it's covered.

Mr. Newfield: When local contractors process a claim, are the benefits paid with Federal funds or are the local contractors paying out those benefits? I'm trying to determine if the local contractors are just administering these plans or profiting from claim determinations.

Dr. Schafer: You'll have to write me about the payment question because it's not my area of expertise. I do know that local contractors do not profit from denying services.

Mr. Newfield: Your requirement that items or services must improve functionality is an important issue for CFS patients because loss of functionality is part of their problem. What, if anything, can CMS do to help this patient population with regard to coverage issues under the paradigm of functionality?

Dr. Schafer: It's to improve the function of a malformed body member. We are all for functionality being improved for patients, but I don't know how to answer the question that you've asked me. We operate under statute. If you want to move the law, go to Congress.

In response to CFSAC members' questions, Dr. Schafer clarified that:

- SSA is the agency that defines "permanent disability" as it relates to eligibility for SSDI.
- The Program Integrity Manual contains the checks and balances on how Medicare operates. The manual is available online.
- The Coverage and Analysis Group does not collect data on CFS. She knew of no ongoing studies or data collection, but would be willing to check into it.
- She agreed to sit in on the Quality of Life Subcommittee meeting to provide information.

Dr. Klimas, noting that CFS researchers have not produced a biomarker on which everyone can agree, asked Dr. Cavaille-Coll if studies that use functionality as a primary outcome would be as acceptable to the FDA as studies that use biomarkers as the outcome. Dr. Cavaille-Coll replied that the FDA is looking for substantial evidence of efficacy and safety based on adequate well-controlled trials. FDA does value functionality because the agency values clinical benefit.

Dr. Jason: Our basic issue is that we've got hundreds of thousands of patients who are not getting the interventions that they need. Do you have a sense of the types of people in the government that might help us as we try to figure out how we can shed light on this problem?

Dr. Schafer: That's a one-billion dollar question that you've asked me, haven't you? I'm going to have to defer comment on that.

In response to committee questions, Dr. Schafer clarified that:

- NCDs can be requested by local contractors.
- NCDs can be requested for novel treatments.
- A CMS/FDA parallel review has been discussed but isn't currently being done.

Dr. Oleske: Some of the treatments for Lou Gehrig's disease are also effective for CFS patients. Why do we have a system that will allow one patient to be treated and another denied treatment that may help their condition? People with chronic illnesses need services, and when you start picking and choosing the disease based on who is famous and got the disease, it is bothersome. How can CFSAC help ensure that the CMS process does not end up denying patients with chronic diseases who may need to receive services even if they don't have a defined illness like Lou Gehrig's disease?

Dr. Schafer: I understand your concern, but I'm going to go back to Congress, what they've mandated and how it's been interpreted.

Dr. Oleske: So all we can do is go to Congress, and if we had the power and influence, ask for CFS to be added to the exception list?

Dr. Schafer: Yes.

Ms. Healy expressed concern over consistency in treatment now that CMS contractor determinations will be made on a more regional basis. She noted that if the system is designed for more consistency, that consistency should reflect what is best for the patients. She expressed concern over whether the CMS process would result in the best treatments being covered in all 15 regions. Dr. Schafer emphasized that ineffective or unfair variations among local coverage determinations is one of the reasons that somebody would get a national coverage determination based on evidence.

Dr. Bateman commented that Medicare is most consistent in coverage and it is a great relief for her when patients qualify to get disability. She said that she is grateful that Medicare provides a safety net for CFS patients once they get past the hurdle of qualifying for disability.

Dr. Parekh: We thank you for your appearance today and recognize that some of our concerns are outside your purview. CFSAC has a Quality of Life Subcommittee that includes benefits, claims, and coverage. Any guidance you can give to that subcommittee, even if it's linking them with other individuals, would be very helpful. We'll collect outstanding questions for you and be in touch.

Prudence Goforth, Director, *HHS Web Communications Division*
Accompanying Document: *Chronic Fatigue Syndrome Advisory Committee Web Information*

CFSAC's role is to advise, not advocate. The CFSAC website's role is to provide information on CFS, but it is not a clearing house and must follow government guidance and laws.

CFS on the web:

- There are 12,000 individual blogs specifically related to CFS. Blogs can act as a funnel of information among researchers that evolves to a consensus opinion.
- A Google search produced 1.9 million hits for CFS with CDC listed first, followed by Wikipedia, and the Mayo Clinic.
- HHS Secretary Leavitt is one of the first cabinet officials to blog.
- Other websites with a wealth of information on CFS: CDC, a literature review on AHRQ's website, NIH and ORWH, and SSA.
- Right now all of these are mostly stand-alone silo websites. A searcher might land on any one of these pages, but he or she wouldn't know that there is other information available. HHS will evolve into a more topic-based website so that highlight boxes take searchers to other pages on CFS.

Laws and OMB Guidance on External Linking

- The Information Quality Act says that government websites have the responsibility to maximize quality, objectivity, utility, and integrity of information.
- OMB directs government agencies to limit external linking to information or services necessary for the proper performance of an agency function.
- Agencies must develop a plan of management to ensure that external links remain active and lead to objective information. The public looks to government for credible information. Links are often seen as the agency endorsing whatever information is on that website.
- All government websites must comply with laws mandating access to the disabled.

Committee Member Q&A

Ms. Artman discussed the possibility of videotaping the meeting and making it available for download, noting that this is apparently not financially feasible. She asked whether producing an audio version with a transcript would be less expensive, noting that many CFS patients are too sick to physically attend the meeting and committee members are seeking the most cost-effective way to allow long distance participation.

Ms. Goforth replied that video and audio transcripts are difficult to manage on the website because they have to be offered on demand, made accessible, and meet objectivity rules. She added that any on-demand content is expensive. Ms. Artman asked about the possibility of having a one-time streaming video. Ms. Goforth replied that a webinar would meet that need but is also expensive. She said that an audio feed is not usually effective.

Dr. Parekh outlined three steps that he will take to identify a method for long-distance participation: finding out the preferences of the community, determining the traffic on the CFSAC website, then laying out the different options available.

Ms. Goforth responded to other committee member concerns:

- The question of whether the HHS website can link to the IACFS/ME website is a policy question that HHS officials would need to make based on objectivity guidelines. A management plan would be needed.
- The CFSAC website needs to be updated, including the removal of outdated links. She plans to work with CFSAC to make the site more effective.
- A government website may not link to organizations that also lobby Congress.

Committee members agreed to forgo their break in order to continue their discussions.

Committee members next discussed making ARHQ an *ex officio* member of CFSAC. It was noted that *ex officios* are specified in the CFSAC charter. The committee does not have the power to amend the charter. **Dr. Parekh** said that the committee can recommend that the Secretary consider revising the charter to add ARHQ as an *ex officio*.

Members then agreed to consider several committee recommendations before breaking into subcommittee groups. Mr. Newfield made the following motion, which was approved unanimously:

CFSAC Recommendation

The committee recommends that a representative of AHRQ be added as an *ex officio* member to CFSAC effective immediately, but at least in advance of the next subcommittee meeting.

Mr. Newfield noted that no action has been taken on the committee's May 2007 recommendation that a proposal for a CFS Centers of Excellence be taken to Congress. **Dr. Oleske** commented that CFSAC has been explicitly firm multiple times in its support for CFSAC Centers of Excellence, and it may not serve the committee's best interest to continue pressing the Secretary to act on a recommendation that he has so far obviously rejected. Mr. Newfield expressed disappointment and frustration that CFSAC has not advanced the issue.

Dr. Hanna said that the main issue is really lack of funding for centers and the fact that CFSAC cannot go to Congress and ask for it. She encouraged CFS researchers to make use of existing mechanisms.

Dr. Klimas commented that the desire to provide CFS patients access to quality care is an important reason for pushing for Centers. She suggested clarifying to the Secretary that patients can't find doctors and this is why CFSAC continues to press for Centers. Committee members then discussed other mechanisms that the Secretary could support.

Dr. Oleske asked **Dr. Parekh** if it would be appropriate to recommend that the Secretary support sites of clinical excellence for CFS through mechanisms other than research. Dr. Parekh replied that "other mechanisms" is too vague and the committee should try to be more specific. He continued that it is in the committee's prerogative to repeat the same recommendation again for symbolic reasons, but realistically, it may not have any benefit.

Dr. Parekh also clarified that ARHQ puts together guidelines based on the evidence that's been established through clinical trials. ARHQ centers are collecting evidence, but they're not in the business of actually doing the clinical care and conducting the clinical research. ARHQ takes the information that is provided from academia and private research to produce and critique evidence-based guidelines. ARHQ conducts health services research based on evidence. They do not conduct basic or clinical research.

Recognizing that CFSAC itself cannot lobby Congress, **Dr. Glaser** recalled his experience with winning Congressional support for mind-body medicine through funding of NIH's Office of Behavioral and Social Research. A special study section was created to review mind-body grants, and the office received funding to support five centers at $10 million each for five years. Congress renewed the funding once.

Dr. Glaser emphasized his view that the CFS community must find a similar way to perform focused research on etiology and markers because that is the best way to get the resources necessary to treat CFS. He maintained that if the basic and social sciences similarly focused on CFS for 10 years, they would find markers. "The only way we're going to get this resolved is to deal with the evidence-based medicine issue," he concluded. "That is difficult without etiology and markers. Until we have that, the evidence-based issue is important."

Mr. Newfield noted that Dr. John Agwunobi, HHS Assistant Secretary for Health, has not followed up on his statement at the July 2006 meeting that he would attend at least every other CFSAC meeting. Mr. Newfield suggested that Secretary Leavitt be invited to participate in the next CFSAC meeting so that members can raise these issues in his presence. Dr. Parekh said that he could deliver that message without a committee recommendation.

Dr. Reeves pointed out that the central issue of CFSAC is getting CFS patients access to good health care. He maintained that although research is important, a tremendous amount of information has been accumulated since the 90s, and science is closer to the physiology than is often portrayed. He predicted that there won't be a magic bullet biomarker. He suggested that CFSAC would be more effective if it identified the issues that pertain to access to and utilization of healthcare, then made cohesive recommendations attacking that one objective rather than make piecemeal recommendations.

Dr. Hanna pointed out that NIH has funded grants in the last two years that when finished will presumably produce the kind of answers CFSAC has been discussing, and all of these grants are multidisciplinary.

Committee members continued to discuss the benefits of developing another recommendation on centers. **Dr. Klimas** raised the possibility of working with the HRSA network of primary care clinics to deliver care to CFS patients. **Dr. Willis-Fillinger** responded that while HRSA develops performance measures that are based on evidence, the agency approach to healthcare is generally not disease specific.

Dr. Reeves interjected that the CDC Georgia studies indicate that access to healthcare is not the problem—it is the barriers to using that healthcare. This reinforces that CFSAC should

carefully assess the problems of providers and patients. Access, utilization, treatment and provider education problems suggest different solutions and emphases.

Dr. Oleske interjected that CFSAC could take the time between meetings to formulate recommendations. Mr. Newfield noted that when the patient community reviews the minutes, people will appreciate the committee's concern and take the steps they deem appropriate to present the issue outside of DHHS. Dr. Snell observed that committee members agree that centers are the way to go, but that the money for them is not available. He suggested that CFSAC defer to the groups who can lobby for the money and spend committee time exploring other alternatives.

Committee members questioned Dr. Parekh about Ms. Goforth's statement that CFSAC provides advice and not advocacy and how that fits with the committee's mission of urging the DHHS Secretary to do what is best for CFS patients.

Dr. Parekh replied that CFSAC members have been selected for their expertise on biomedical research, as clinicians, or as patients to provide science-based advice and recommendations to the Secretary and the department. CFSAC is not an advocacy organization. Members can be advocates, but they cannot be individual advocates when performing CFSAC duties. Being a CFSAC member doesn't necessarily preclude work in other organizations. He noted that a knowledgeable HHS ethics official could appear at the next meeting to clarify the rules.

CFSAC Recommendation

Offered by Dr. Snell with the purpose of institutionalizing CFS within CDC:

The Committee recommends that the CDC effort on CFS be restructured to reflect a broader expertise on the multifaceted capabilities required to execute a comprehensive program that incorporates the following elements:

1. An extramural effort directed by the Office of the Director.
2. Sufficient funds for a program for which the authority and accountability is housed at the level of a coordinating center director.
3. A lab-based component that maintains the current search for biomarkers and pathophysiology.
4. The recommendations of the external CDC Blue-Ribbon panel including developing, analyzing, and evaluating new interventions and continuing support for longitudinal studies.
5. An expanded patient, healthcare provider, and family caregiver education effort that is managed by staff with appropriate expertise in clinical and public education strategies.

The recommendation was unanimously approved after committee member discussion that included the following topics:

- Number 1 addresses the fact that when a broad range of expertise is needed, it is difficult to house in one institution. Extramural funding also promotes the healthy exchange of ideas and information by scientists from numerous institutions and attracts more quality researchers.
- Provider education is critical as underscored by the CDC Georgia study statistic that only a third of primary care providers feel that they have sufficient knowledge to diagnose CFS. When the SG letter goes out, resources to follow up on provider interest must be in place.
- The statement in support of education efforts must encompass all groups and make clear that such efforts should be expanding.
- Wording to add language about the Blue Ribbon report and the continued support of longitudinal studies is important.

[Dr. Oleske called a break for lunch.]

When CFSAC reconvened, members adjusted the agenda so that one public comment would be followed by a 15-minute breakout for subcommittee discussions then a full committee discussion.

Marly Silverman, CFS patient

I don't want you to worry so much whether there's funding for Centers of Excellence or other programs. I really would like you to concentrate on the fact that your expertise is extremely important to us as patients because it will actually guide my future, the future of my medical care, and the future of thousands and millions of other individuals with CFS in this country. Thank you for the good work.

Dr. Oleske: Thank you and we take that to heart. Although you hear us talking about the practicalities and limitations of funding, I think that you can also see that we really don't let that negate the recommendations that we have made so far. It is good to be reminded that our job is to make recommendations for patients with CFS. We're not the funders; we don't raise the money. We just give our expertise on what the care should be.

[Dr. Oleske suspended the meeting for 15 minutes to accommodate subcommittee discussions]

[Dr. Oleske reconvened the meeting.]

The subcommittees presented their future plans, including what they would like to be taken up at the next CFSAC meeting.

Research

Dr. Jason: We continue to be most interested in looking at the big picture trying to understand how different sources of funds are being generated and used in different agencies, particularly NIH and CDC. We had a list of questions for CSR and we're hoping to continue to get information. We have a good dialogue going with them now, so we'll continue that in preparation for the May meeting. We also hope to have more funding information from NIH and CDC. We have asked Drs. Reeves and Hanna to work with us on this.

Education

Ms Healy: We would like to continue to work on that package idea related to the SG letter and provide ideas for how to implement it and to whom it should be sent. We would like to offer assistance to Ms. Goforth for the CFSAC website. We would like her to participate in our next meeting and give her some information from our perspective on how the website could be more user-friendly.

We also would like to collaborate on a toolkit for family healthcare givers.

Dr. Klimas read the subcommittee's proposed recommendation:

Committee Recommendation

The committee recommends that the Secretary use CFS to develop and implement a model that would fast track within the DHHS family of agencies mechanisms that would meet the needs of people with complex chronic multi-system illnesses that require a multidisciplinary collaborative approach. We suggest DHHS develop a department-wide multi-agency task force that can establish a plan to alleviate the suffering of people with this illness.

This should include but not be limited to:

1) **Increase the evidence base through basic and clinical research (etiology, biomarkers, pathophysiology, natural history, and effective treatment).**
2) **Solidify evidence and develop clinical guidelines for treatment practice.**
3) **Develop education and clinical training (evidence-based) of health care providers.**
4) **Provide evidence-based information and support to patients and families.**
5) **Ensure access to quality and appropriate care.**

The working group should report progress on the development and implementation of this model to the Secretary on a regular basis.

The recommendation was unanimously tabled due to member concerns raised during the discussion. These concerns are summarized below:

- This recommendation may only lead to the formation of a task force consisting of the five CFSAC *ex officios* and several other representatives from the department who would only review the CFSAC recommendations and put together a report. The recommendation must stimulate actual outcomes. It must move DHHS agencies to work together on something. The goal is not a report of what's going on, but a task force that solves a problem.

- The problem to be addressed is the vicious cycle that CFSAC confronts at every meeting: We have patients who have no clinical care. They have no clinical care because we have no evidence-based medicine to treat them that would be acceptable to payers. We are stymied in our research because we don't have enough patients in any one place to do the large-scale clinical trials we need to develop the evidence-based treatment approaches. The intent of this recommendation is to find the resources within HHS that could immediately start to implement clinical access for these patients and help develop through interagency coordination the clinical research networks that would give us the evidence-based medicine we need to better treat our patients. We want the Secretary to embrace the idea of making structural changes to resolve the bigger issue: access to care.

- The recommendation should make a more positive statement using action words. Perhaps we should suggest it to the Secretary as a Roadmap Program.

- The recommendation should state our desired outcome in the form of concrete goals. The five items listed seem redundant with what CFSAC is already doing.

- We want to see treatment trials with therapies evaluated. We should consider how to better prompt FDA to pressure drug companies—particularly the developer of Ampligen, who is withholding research. There needs to be some sense of urgency that we need treatment for this disease. We need to stimulate development of treatment plans and diagnostic plans that others could use.

- The recommendation should not list tactical actions without fleshing out strategic goals. The strategic goal is to develop a model that works and that DHHS can use in dealing with chronic multi-system complex illnesses like CFS and FM.

- We have to start treating people right now. We have people who are sick with symptoms, and that's what we need to address with strategy. Treating people is what will eventually produce the etiological agents.

- Clinicians should be concerned that the task force as proposed is composed only of government agencies representatives.

- CFS has already been brought up within NIH as a model for multi-systemic illness and the idea hasn't been taken up.

- CFSAC members have had a concern that CFS would be overshadowed under the NIH Roadmap by FM, interstitial cystitis, and other multi-systemic diseases. This recommendation seems to pose the same problem.

- How does the recommendation relate to the NIH Roadmap?

- CFSAC must seriously consider the comments from the two subject experts on how HHS and NIH work and use them to amend the recommendation.

- There is a danger that the recommendation as worded would end up evolving into a coordinating committee when its intent is to advocate for a new paradigm of attacking chronic illness. Right now it is addressed in silos to some extent. We need a way to make sure that we're all working together and that is more than just coordination. We want to inspire doing, not just talking.

- We need to couch our recommendation by modeling for chronic diseases. We could craft this in a way that we meet our obligation to the CFS community and put forth CFS as a model while broadening it to address the fact that right now in the United States, we do not fund what is needed by chronic diseases.

Dr. Klimas requested that Dr. Reeves present more information at the next CFSAC meeting on Georgia study statistics on the provider survey and on patient access to healthcare.

Public Comment

Kim McCleary, President and CEO, *CFIDS Association of America* [Commenting on the just-tabled recommendation]

Perhaps the committee should consider recommending when NIH rewrites it's PA [parent announcement] that one of the emphases should be to accrue and strengthen the evidence base for treatment guidelines. There's a huge amount of information collected over the past five years about what the provider education initiative has taught us. That is one example of the data that is available, but is not being looked at in a way that we can translate into action and policies at all the agencies working with CFS. So much could be learned from what's out there already —perhaps through better communication and coordination.

Marianne Lumly, the mother of a child with CFS

The issues being addressed by the recommendation are not unusual. They are addressed by complex organizations all the time. There are models out there, including Johns Hopkins' efforts to integrate its research, education, and clinical programs.

My daughter got sick at the end of high school for six weeks and was eventually diagnosed with FM. She went off to college and stayed a year and a half. When she came back, she

was hit with a serious form of CFS that left her barely able to raise her head. The worst part of seeking treatment is the bias that CFS is a psychiatric illness.

When I heard you talking about childhood trauma, bells went off in my mind. Imagine going into a doctor's office with your child barely able to raise her head and having her be asked about her childhood. Will that elucidate the underlying cause or lead to a cure? Probably not. Put the psychological research in the context of the overall disease and be careful how you say it, because you could set back progress.

Quality of Life Subcommittee report

Ms. Artman

- We were pleased that CMS could come. Dr. Schafer said that any questions that CFSAC members have on CMS can be emailed to Dr. Parekh or me, and we will forward them to her for a solid answer.

- CFSAC can do nothing to expedite FDA's drug approval process. FDA has a fast-track program and drug companies are welcome to apply for it. Drugs for diseases that are rare—like CFS—can be fast tracked, but it's up to the drug company that is producing that drug to apply for that fast track program. Our hearts go out to you in all of your suffering, but CFSAC has no power to do anything for you.

Items for Future CFSAC Meetings

- The patients' bill of rights and how that applies to CFS patients.
- ADA compliance issues in relation to pediatrics, specifically children who are not able to go to school or are in college and need dorm rooms on first floor and who are having issues with their needs being met.
- Conducting a quality of life survey using Dr. Jason as a source to feed us some of the surveys that have already been done.

The most important thing that we can do as a quality of life subcommittee is support evidence-based research so that tests can be completed and drugs can be approved. Evidence-based research is the most important thing for a patient's quality of life. Once there's a biomarker that can be tested for, it will give us a peace of mind that cannot be explained. We'll be able to point to something and say, "This is my illness." That's what gets us clinical trials, drugs, and eventually, effective treatment.

Adjournment

Dr. Oleske thanked those who attended the meeting, especially CFS patients and their families, and agency members who spent extra time assisting the committee. He said that CFSAC will work until the May meeting to accomplish some of the goals that members set

out, especially the task force recommendation. **Dr. Parekh** thanked CFSAC members and members of the public. Dr. Oleske adjourned the meeting.