CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE

Meeting

Monday, May 5, 2008
9:00 a.m. to 5:30 p.m.

Tuesday, May 6, 2008
9:00 a.m. to 3:00 p.m.

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

Agenda Monday, May 5, 2008

9:00 a.m.	**Call to Order** **Opening Remarks**	p. 7	Dr. James Oleske *Chair, CFSAC*
	Roll Call, Housekeeping	p. 7	Dr. Anand Parekh *Designated Federal Official*
9:30 a.m.	**Centers for Disease Control and Prevention Update**	p. 7	*Ex-Officio*, CDC and CDC Representatives
11:00 a.m.	**Subcommittee Breakout Discussions**	p. 30	Committee Members
12:00 p.m.	**Lunch**	p. 30	
1:00 p.m.	**Subcommittee Updates (30 minutes each)**	p. 31	Subcommittee Chairs and Committee Members
	1. Education	p. 32	
	2. Research	p. 31	
	3. Quality of Life	p. 33	
2:30 p.m.	**Health Resources and Services Administration Update**	p. 46	*Ex-Officio*, HRSA and HRSA Representatives
3:30 p.m.	**Social Security Administration Update**	p. 54	*Ex Officio*, SSA and SSA Representatives
4:30 p.m.	**Public Comment**	p. 64	Public
5:30 p.m.	**Adjournment**	p. 71	

Agenda Tuesday, May 6, 2008

9:00 a.m.	**Call to Order** **Opening Remarks**	p. 72	Dr. James Oleske *Chair, CFSAC*
	Roll Call, Housekeeping	p. 72	Dr. Anand Parekh *Designated Federal Official*
9:15 a.m.	**National Institutes of Health and Food & Drug Administration Update**	p. 72	*Ex-Officio*, NIH and NIH Representative; and *Ex-Officio*, FDA
9:45 a.m.	**Public Comments**	p. 76	Public
10:30 a.m.	**Office of the Surgeon General—Provider Education**	p. 88	Representative of the Office of the Surgeon General
10:45 a.m.	**New Jersey Medical Student Scholarship Presentation**	p. 90	Dr. Ken Friedman
11:00 a.m.	**Subcommittee Breakout Discussions**	p. 100	Committee Members
12:00 p.m.	**Lunch**	p. 100	
1:00 p.m.	**Committee Discussion**	p. 100	Committee Members
3:00 p.m.	**Adjournment**	p. 105	

CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE

Voting Members

Chair

James M. Oleske, MD, MPH, CIP Newark, NJ	Term: 01/03/06 to 01/03/09
Rebecca Artman Middleburg, FL	Term: 01/03/06 to 01/03/09
Lucinda Bateman, MD, PC Salt Lake City, UT	Term: 01/03/06 to 01/03/09
Ronald Glaser, PhD Columbus, OH	Term: 04/01/07 to 04/01/11
Arthur J. Hartz, MD, PhD Iowa City, IA	Term: 04/01/07 to 04/01/11
Kristine Healy, MPH, PA-C Chicago, IL	Term: 01/03/06 to 01/03/09
Leonard Jason, PhD Chicago, IL	Term: 04/01/07 to 04/01/11
Nancy Klimas, MD Miami, FL	Term: 04/01/07 to 04/01/11
Jason Newfield, Esq. Garden City, NJ	Term: 07/01/06 to 07/01/09
Morris Papernik, MD Chicago, IL	Term: 01/03/06 to 01/03/09
Christopher Snell, PhD Stockton, CA	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 (ORWH)

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
Deputy Assistant Secretary for Health (Science and Medicine)
Office of Public Health and Science

Speakers

Centers for Disease Control & Prevention (CDC) Staff
J. Michael Miller, PhD, (D)ABMM, Associate Director for Science, National Center for Zoonotic, Vector-Borne, and Enteric Diseases (NCZVED), CDC
Sarah Wiley, Associate Director for Policy, NCZVED, CDC
Fred Fridinger, DPH, CHES, Project Officer, CFS Public Awareness Campaign, Marketing and Communication Strategy Branch, Division of Health Communication and Marketing, National Center for Health Marketing, CDC

Health Resources and Services Administration (HRSA) Staff
Dr. Daniel Mareck, Chief Medical Officer, Bureau of Health Professions, HRSA

National Institutes of Health (NIH) Staff
Dr. Cheryl Kitt, Deputy Director, Center for Scientific Review, NIH

Social Security Administration (SSA) Staff
Sharon Shreet, Senior Advisor to Office of the Associate Commissioner, Office of Employment Support Programs
Fran Huber, Social Insurance Specialist, Office of Compassionate Allowances and Listings Improvement, Office of Disability Programs
Mark Kuhn, Social Insurance Specialist, Office of Compassionate Allowances and Listings Improvement, Office of Disability Programs

Monday, May 5, 2008

Call to Order/Opening Remarks

Dr. James Oleske

Dr. Oleske called the Chronic Fatigue Syndrome Advisory Committee (CFSAC) meeting to order, expressing appreciation for voting members' consistent attendance and *ex-officio* representatives' loyalty and steadfastness in supporting CFSAC.

Roll Call, Housekeeping

Dr. Anand Parekh

Dr. Parekh welcomed CFSAC members and the public, noting that the information contained in committee members' meeting folders was also available to the public at the back of the meeting room.

Dr. Parekh conducted roll call and confirmed that a quorum was present, with 9 of 11 voting members in attendance (Drs. Arthur Hartz and Nancy Klimas were absent. Dr. Hartz joined the meeting after the first speaker's presentation). Four out of five *ex-officio* members were present (Dr. Laurence Desi of SSA was absent).

Dr. Parekh then discussed the day's agenda and the items in CFSAC members' meeting folders including:

- The CFSAC Charter.
- A list of committee members.
- Minutes from the November 2007 CFSAC meeting. Dr. Parekh asked that committee members review the minutes for accuracy before Tuesday's approval vote.
- Written materials to accompany the oral presentations of CDC, HRSA, and SSA.

- Testimony of CFS patients who registered by May 1 to make oral comments at the meeting.
- A folder of the public comments and testimony that were sent to CFSAC via email.

CDC Update

Dr. J. Michael Miller, Associate Director for Science, *National Center for Zoonotic, Vector-Borne, and Enteric Diseases (NCZVED), CDC*
Sarah Wiley, Associate Director for Policy, *NCZVED, CDC*

Dr. Miller conveyed greetings from Dr. Lonnie King, Director, NCZVED, and Dr. Mitchell Cohen, Director of the Coordinating Center for Infectious Diseases, and told CFSAC members that both directors are engaged in CFS issues.

Dr. Miller displayed a CDC organizational chart and explained where CFS is addressed within the reorganized agency:

- Communication and training efforts are generated from the Coordinating Center for Health Information and Service, National Center for Health Marketing, Division of Health Communication and Marketing.
- The laboratory component is housed within the Coordinating Center for Infectious Diseases, NCZVED, Division of Viral and Rickettsial Diseases, Chronic Viral Diseases Branch.

Dr. Miller continued:

The target CDC appropriation for work specifically related to CFS is $4.8 million annually for FY 2006-2008. The actual appropriation has been somewhat less. In Dr. Reeves's group, this supports 13 full time equivalents (FTEs), 17 contractors, and all program research and activities. Skill sets available for these activities include:

- Surveillance (populations and registries).
- Epidemiology.
- Genomics and proteomics (laboratory measurements and analysis).
- Clinical studies involving psychoneuroendocrinology, immunology, sleep physiology, and treatment trials.
- Behavioral scientists.
- Biostatistics, Bayesian statistics, and mathematical modeling.
- Education and public health communications in collaboration with the National Center for Health Marketing.

As a result of such skill sets, this group produced 31 publications in 2006; 15 in 2007 (four in press); and 5 in 2008 (one in press, six in review). The review process is lengthy because the studies are large and complex.

The breadth of CDC outreach for external partnerships and collaborations has produced the following (with many still in process):

- Emory University
- Miami University
- Ohio State University
- Mayo Clinic
- Stanford University
- University of Illinois

The $4.8 million funding target does not cover all the funding that is made available at CDC for CFS. Some $5.5 million was added for FY 06-09 for the CFS Public Awareness Campaign in the Marketing and Communication Strategy Branch. This includes funding allocated to the CFIDS Association of America for its public awareness campaign. About $900,000 remains to be allocated.

CDC External Peer Review of CFS Program

CDC plans to conduct an external peer-review of the CFS program in late summer/early fall 2008. This review will be conducted by a panel composed of national and international experts that is to include representatives from the Coordinating Center for Infectious Diseases Board of Scientific Counselors and CFSAC. CDC is requesting that CFSAC members recommend names of experts with no conflict of interest (direct funding from CDC) who could sit on a panel to:

- Review program goals and objectives. This will include a candid and open review of the direction of research. The panel will produce a formal written report that will be taken seriously by all CDC directors.
- Review program outputs and outcomes as well as comment on the future directions in which CDC should or should not be going.
- Provide specific feedback to aid prioritization of CDC efforts, including CFS communication and research efforts.

Dr. Miller offered himself, Ms. Wiley, and Dr. Reeves as conduits for any CFSAC questions for the CDC and pledged clear and open communication lines to better facilitate answers. He directed policy and budget questions to Ms. Wiley and research questions to Dr. Reeves, and then introduced Dr. Reeves as the next speaker.

Prompted by a question from **Dr. Jason**, **Dr. Oleske** established that both Dr. Miller and Ms. Wiley would be available at the end of the full CDC update to answer questions. Dr. Oleske also noted that **Dr. Hartz** had joined the panel.

Dr. William Reeves, Chief, *Viral Exanthems and Herpesvirus Branch*
National Center for Infectious Diseases, CDC
Accompanying Document: *CDC CFS Program Update May 2008*

Dr. Reeves noted that members requested at the November 2007 CFSAC meeting that he provide information about CDC activities dealing with quality of life; provider education; and knowledge, attitudes, and beliefs (KAB) of both providers and the general public. He continued:

CFS in the United States

The CDC CFS studies in Georgia used a sensitive screening method and a sensitive and specific confirmatory method to estimate that about 2.5% of the population suffers from CFS. If that rate is extended to the U.S. population, it would mean that 4 million people have CFS. Dr. Jason's population surveys in Chicago—as discussed in his most current publications—estimate that about .5% suffer from CFS. If that rate is extended to the whole United States, it equals 1 million CFS cases. The actual number of cases is probably somewhere in between these two estimates. The "body count," however, is not as important as what is happening to those people who have the illness.

Quality of Life

About a quarter of the people with CFS who are detected in population surveys are unemployed or receiving disability.

Economic Impact of CFS – Indirect Costs (lost employment and earnings)

- CDC has now done two studies and is in the process of evaluating the one in Georgia. The studies were done with sophisticated economists. CDC estimates that the average family in which someone suffers from CFS forgoes between $15,000-$20,000 annually in earnings and wages. When you consider that the median household income in the United States is about $40,000, the average family in which someone has CFS is forgoing about half of the median annual income. When these numbers are projected to the whole United States, CFS costs the U.S. economy about $9 billion annually.

- Individuals with CFS have a 19 percent lower probability of being employed.

- Early onset of CFS significantly reduces educational attainment. If a person develops CFS when he/she is younger than 25 years old, his/her probability of completing a college degree drops from 50 percent to 25 percent.

Economic Impact of CFS – Direct Costs (healthcare utilization and expenditures)

- The Georgia study has found that the average individual with CFS spends about $2,500 more per year than a well individual. Most of that is going to provider encounters. About two-thirds less is going to medications and over-the-counter products.

- Dr. Jason has recently published a study from his Chicago survey that shows expenditures of $1,200 more per year from his population cohort than well individuals. His study shows that this was primarily paying for medications and over-the-counter materials.

There are significant costs from CFS in earnings and wages; in one's ability to achieve one's maximum potential in life; and for medications, drugs, and medical care. CDC does not believe that these costs can be extended to the U.S. population. Regional surveys are based on regional costs. Those costs are quite different around the country. CDC does not believe that regional study information can be extended to say that $60 or $80 or $100 billion is being spent in the United States.

CFS in the United States (continued)

Besides the CDC estimate of 4 million Americans with CFS, there are an estimated 7 million who report CFS-like symptoms. Fewer than half of those 7 million have consulted a physician and between 40 and 50 percent have an undiagnosed, treatable medical or psychiatric condition of which they are not aware.

When that 40-50 percent is brought into a clinic, the following exclusionary diagnoses (among others) are discovered:

- Thyroid disease – 24 percent
- Anemia – 18 percent
- Maturity onset diabetes – 14 percent
- Substance abuse – 43 percent

These are all serious conditions for which there are treatments, and yet those people are not seeing providers. The average person with CFS has been sick an average of 5 years. We know that the probability of recovery is certainly higher in the early stages of the illness, and it is negatively associated with how long a person has been ill, how sick he/she is, and the number of symptoms.

Although there is no firm evidence base for saying that if by getting these individuals into a doctor it will improve them, it does make a certain logical sense. The earlier in one's illness that one can begin occupational therapy, physical therapy, and/or cognitive behavioral therapy, the less co-morbidity there is. It is easier to deal with an individual who has been sick a year than someone who has been sick for five or six years.

Provider Education

CDC has been involved in a provider education program since 2001. The 2001-2007 period was largely exploratory with diffuse outreach and material development to determine how to build a provider education program. It cost about $3.8 million over that time period to support the contract. That does not include FTE and in-house costs. Education accounted for 11 percent of our total research allocation.

Provider education had four components:

1. Train-the-trainer – Efforts consisted of setting up exhibits at professional conferences, offering free Continuing Medical Education (CME) courses, conducting grand rounds, and marketing these opportunities. The train-the-trainer program was discontinued in 2004 due to:

    - Lack of sustained interest by the core trainers.
    - Low rate of core trainers conducting follow-on training.
    - Expense of train-the-trainer workshops.
    - Effort required to maintain the program.

2. Professional conferences – CFIDS had booths at 55 conferences from 2003-2007 that resulted in:

    - 12,000 booth visits.
    - 24 conference presentations with about 1,300 attendees.
    - Distribution of 32,000 copies of printed materials. Seventy-two percent of these were a popular laminated resource guide.
    - Distribution of 4,240 print CMEs, with only 5 percent completed—a "dismal" rate.
    - Distribution of 870 video CMEs with only 2 percent completed.

    Marketing expenses were about $500,000 over that time period. One has to begin to question whether 12,000 booth visitors and a very low CME rate are worth that expense.

3. Grand rounds – CDC and CFIDS tried to interdict CFS into medical school curricula by:

    - Giving 29 presentations at 10 venues from 2005-2007.
    - Reaching about 1,370 attendees.
    - Attempting to obtain KAB, with a "dismal" response rate.

4. Developing CME Curriculum – CDC worked with CFIDS to produce:

    - 3,000 CME web hits between 2003 and 2007.
    - A 42 percent certificate award rate. When compared with conference statistics, this percentage demonstrates that CMEs are important and really need to be done over the Web.

    The contract with CFIDS lapsed at the end of 2007. CDC has continued operating CMEs through the first quarter of 2008. The hits have doubled and the completion rate has gone from 42 percent to 60 percent. CMEs are working well *and* we have significant cost savings.

Knowledge, Attitudes, and Beliefs

What do we need to teach providers? In order to answer that question, CDC asked questions through DocStyles—a large, population-based national survey that the agency licenses. CDC also obtains information at conferences, from focus groups, and through a CDC-sponsored CFIDS survey conducted by the Winston Group.

CDC obtains information for its consumer Public Awareness Campaign by licensing HealthStyles, a consumer-oriented survey that is similar to DocStyles.

DocStyles 2006 and 2007:

- A web survey based on a random sample.
- Has a panel of about 142,000 physicians from which the random sample is taken.
- In 2006, sampled 1,250 primary care doctors and pediatricians.
- In 2007, sampled 1,502 primary care doctors, pediatricians, and OB/GYNs.

DocStyles showed that 42 percent of providers nationally have diagnosed CFS. The 2006 & 2007 survey also showed that:

- Virtually every physician has heard of CFS (97 percent in 2006; 96 percent in 2007)
- Virtually all physicians agree that CFS impairs a person's quality of life (87 percent/90 percent).
- Only 20 percent in 2006 and 19 percent in 2007 think CFS is in the patient's head.

There are some problems, though:

- About half (43 percent/50 percent) believe that treatment options are available.
- About 30 percent (25 percent in 2006) believe that there is enough information to treat and diagnose CFS.

These are the problem areas. These are the KABs that we have to address. When DocStyles queried physicians' knowledge of CFS symptoms, the following four came out at the bottom of the results. Physicians do not believe them to be CFS symptoms:

- Vomiting – 5 percent/6 percent
- Excessive thirst – 5 percent/6 percent
- Rash – 5 percent/5 percent
- Hematuria – 2 percent/1 percent

Although physicians may not understand how to diagnose CFS, they pretty much understand the case-defining symptoms:

- Unexplained fatigue not improved by rest – 94 percent/92 percent
- Unrefreshing sleep – 89 percent/88 percent

- Impaired memory/concentration – 82 percent/80 percent
- Muscle or joint pain – 84 percent/80 percent
- Headache – 68 percent/63 percent
- Tender Nodes – 43 percent/44 percent
- Sore Throat – 38 percent/35 percent

The information from CDC meetings and focus groups are pretty much in line with DocStyles results:

- Forty-two percent of practitioners have given a diagnosis.
- MDs and osteopaths are more likely than physician assistants or nurse practitioners to have diagnosed CFS.
- Knowledge regarding symptoms is equivalent to that in DocStyles.
- Practitioners believe that CFS is more difficult to diagnose and treat than other illnesses.

HealthStyles 2006 and 2007

2006 – 5,119 participants
2007 – 4,242 participants
In contrast to practitioners, 62 percent of the public has heard of CFS.
In contrast to practitioners, the majority of the public does not understand what constitutes the illness. This is an area that needs to be worked on.

One interesting DocStyle result that pertains to the awareness campaign and to how we get messages out: hardly any physicians had heard about CFS in the last few months (16 percent/20 percent). They are not being reached. When physicians do hear about CFS, they do so via professional journals (61 percent/60 percent), the Internet (38 percent/37 percent), and continuing education (27 percent/27 percent). TV, radio, and the photo exhibit are not getting to providers. One may need to question whether it is worthwhile to continue trying to reach physicians through these venues.

In HealthStyles, only 11 percent of the general public in 2006 and 10 percent in 2007 had heard of CFS in the last few months. About half of respondents hear about CFS on TV and half in consumer magazines. Internet, radio, and the photo exhibit are not reaching the general public. Based on information from HealthStyles and the Winston group, public awareness of CFS has remained stable since 2003.

CDC CFS Website

The CDC CFS website has received about 5 million page views during 2006-2007 and gets about 6,000 page views a day. It is the 35th most popular of the agency's 200 websites. The sites that beat CFS in popularity include those on STDs (9 percent of traffic), nutrition (8 percent), Medicare/Medicaid services (7 percent), and traveler's health (6 percent) followed by the National Center for Health Statistics, vaccines, and *Morbidity and Mortality Weekly Report*. CFS accounts for about half a percent of traffic, which is similar to the rate for

malaria, Lyme disease, diabetes, cancer, and West Nile virus. The CFS website attracts a healthy portion of CDC traffic.

An analysis of the spikes in CFS web traffic showed that they occurred concurrently with:

- April 2006 - A special issue of *Pharmacogenomics* and a related press conference.
- June/July 2006 – A redesigned CFS web page to support the Public Awareness Campaign, a feature on the CDC home page, and a press release.
- October/November 2006 - Launch of the Public Awareness Campaign at the National Press Club. This constituted the largest spike at about 150,000 page views, but did not last long.
- January/February 2007 – International Association for CFS meeting and related press; three CFS ads.
- June-October 2007 – Seven CFS ads.

When CFS web traffic was analyzed by location, California, Texas, and New York showed the greatest interest at more than 150,000 page views. This was not surprising because these are the most densely populated areas.

When CFS web traffic was analyzed by visiting density based on the page views/Internet population, the following areas showed the greatest interest:

- Bethesda, MD (home of NIH, ranked highest)
- Georgia (home of CDC)
- North Carolina (home of CFIDS Association of America)
- New Jersey
- Minnesota (home of the Mayo Clinic)
- Kentucky

The West Coast and middle of the country exhibited less interest than one might think. Awareness campaigns may need to target these areas more.

The CDC CFS website offers four general areas of interest:

- Information for patients and caregivers (55 percent of traffic).
- Information for healthcare professionals (29 percent).
- News and highlights that include current CDC research publications and brochures (5 percent).
- The Public Awareness Campaign (3 percent).

The most viewed consumer topics are Basic Facts, Treatments, and Symptoms.
The most viewed professional topics are Symptoms, Toolkit: Fact Sheet, and Treatment.

CDC makes all of the agency's publications available on the website and includes executive summaries to enhance public understanding. CDC also makes a concerted effort to publish

in open access journals where articles are not copyrighted. This means that users can access entire articles.

The CFS items attracting the most views are the new publications. A major highlight of the Web use analysis has been that CFS publications are being viewed at a rate equivalent to *BMC Genomics*, a popular primary open access journal with a high impact factor (4.6). This indicates that CDC is on the right track with publishing in open access journals and should publish even more.

The top three *referrer types* to the CDC CFS website were:

- Search engines (71 percent).
- Other websites (16 percent).
- Bookmarks (12 percent). Bookmarks indicate persistent site users.

The top three *search engines* for CDC CFS publications were Google.com, Yahoo, and MSN. The CDC CFS website is the first listing when users type "CFS" into any of these engines.

The top three *referral websites* were:

- NIH (27 percent of traffic).
- Google.com (non-search engine site, 27 percent).
- AOL.com (non-search engine site, 6 percent).

Leading referral websites for the CDC CFS home page were:

- Google.com (24 percent).
- AOL.com (5 percent).
- Mayoclinic.com (4 percent). CDC is currently initiating collaboration with the clinic, whose website also has direct links to each one of the CDC CFS pages.
- NIH.gov, which also directly links to each of the four sections listed below.
- Comcast.net (4 percent).
- CFIDS.org (3 percent). The reason for this organization's low percentage was unclear and needs an explanation.

NIH.gov led all other organizations in referrals to the following four CDC CFS sections. The second-ranked referral websites—listed below after each section—revealed interesting facts about usage:

1. CFS Basic Facts – 50plus.com, a website for those over 50 years of age.
2. CFS Treatment Options: Coping & Managing – about.com, a site for those under 50 who are interested in health and nutrition.
3. CFS Possible Cause – about.com.
4. CFS Who's at Risk – care2.com, a group interested in environmental exposures.

Public Awareness Campaign

There are four media types in the public awareness component of the web page.

- Two brochures available to download and print. CDC did not think that they would get many hits because they are not generally very popular on a web page.
- Public Awareness Campaign photo exhibit.
- Public Awareness Campaign public service announcements.

We were surprised that virtually the only media types downloaded were the brochures. A distant second was the photo from the photo exhibit, followed by the video, the 60-second radio spot, and the 30-second radio spot.

In analyzing the impacts of the Public Awareness Campaign, CDC looked at the average website hits the five weeks before, the three weeks during, and the five weeks after the campaign. Hits went up 202 percent during the campaign and although they dropped off, post-campaign hits remained 25 percent higher that they had been before.

When CDC analyzed the percentage increase in page views based on geographical changes, it found that the campaign had influenced many of the areas of the United States—including the middle of country—that had previously had a low awareness.

When CDC analyzed the campaign's impact on users' interests measured by page views, it found that hits on the Public Awareness section went up by a miniscule amount and CFS publications remained level, but there was a 29 percent increase in hits on the Consumer Section and a 72 percent increase in hits on the Professional Section.

Many of the page hits dropped from their peak in the post-campaign period, but have remained at a higher level than their pre-campaign hits. Diagnostic Symptoms, for example, has remained quite high. Possible Causes and Diagnosing CFS are also higher than they were at the pre-campaign baseline. Some pages have gone down, however, including Basic Facts and Symptoms of CFS. Some of the drop may be due to the fact that people already know about the basic facts and symptoms as shown in the KAB results.

Conclusions

- CFS causes considerable population morbidity.
- Education of providers, patients, and caregivers is needed to reduce that morbidity.

Provider Education

- Train-the-trainer is not effective for CFS.
- Meetings/conferences are expensive. Although many items can be handed out, there is no outcome measure and these gatherings are not a good venue for CME.
- Grand rounds are expensive in terms of time and dollars, but they do inject CFS into medical school curricula and make effective changes in KAB.

- Web-based CME is cost effective, carries the authority of being on a .gov website, has certification, has a high (60 percent) completion rate, and allows CDC to directly measure KAB so that CME can be tailored to exactly what people need to know.

Provider Awareness

- 97 percent of physicians have heard of CFS.
- Most of them get their information from professional journals, which allows CDC to provide the articles on its website.
- Only 16-20 percent of physicians have heard of CFS in the past few months.
- Newspapers, meetings, TV, radio, and the photo exhibit are irrelevant to practitioners.
- Doctors know that CFS is a serious disease.
- Most physicians (80+ percent) know the defining symptoms.
- About half of doctors have diagnosed CFS.
- Very few doctors think that “it’s all in the head.”
- Doctors want information concerning evaluation, diagnosis, and treatment.

Public Awareness

- 62 percent of the public has heard of CFS.
- This percentage has not changed from 2003-2007.
- Only 10-11 percent of the public has heard of CFS in the past few months.
- This has not changed over the last two years.
- The most common means for the public to hear about CFS are TV, magazines, and newspapers.
- Internet, radio, and the photo exhibit would appear from the data to be largely irrelevant.
- About half of the public think that CFS is real and is a serious illness.
- Fewer than half know the defining symptoms.

CDC CFS Web Page Use

- 35th most popular of all CDC web pages.
- Spikes have occurred in relation to the Public Awareness Campaign.
- In general, usage rapidly returned to previous levels.
- Views to diagnosis, causes, and risk factors remain high; views to the Professional Section show the greatest increase.
- The Consumer Section is the most popular, with treatment and symptoms the most popular pages.
- The Professional Section generates 29 percent of page views and users are downloading those items that CDC expected—Toolkit, fact sheet, treatment, and publications.
- Four media types can be viewed/downloaded and the two print formats are by far the most popular (Understanding CFS & the Toolkit).

- The photo exhibit and the public service video and audio are not used to an appreciable extent.

Dr. Reeves noted that he is providing information that CDC is working on and that figures and interpretations may change. He emphasized that the data is not finalized, but provided copies of his slides to CFSAC members and the public.

Fred Fridinger, DPH, CHES, Project Officer, CFS Public Awareness Campaign, ***Marketing and Communication Strategy Branch, Division of Health Communication and Marketing, National Center for Health Marketing, CDC***
Accompanying Document: ***Chronic Fatigue Syndrome Public Awareness Campaign Update***

Dr. Fridinger noted that he was appearing before CFSAC for the third time and thanked Drs. Miller and Reeves for their presentations. He then proceeded with his update of the CDC CFS Public Awareness Campaign:

Besides himself as Project Manager, he has one other person on staff who assists with the campaign itself. DocStyles and HealthStyles are coordinated through the Porter Novelli market research firm. The monies that come down to support public awareness do not go toward supporting salaries.

The CFS Public Awareness Campaign

- Timeline started with the media launch in November 2006 and will continue through September 2009.
- Focus has been on women 35-55 years old and primary care physicians.
- Marketing research, message and materials development, and testing all occurred pre-launch. Since the media launch, CDC has continued with paid advertising, the photo exhibit tour, and coordination with various professional organizations.
- The campaign theme has focused on the recognition of CFS signs and symptoms, becoming informed about the disease, and seeing a physician to get diagnosed.
- The campaign's continuing call to action:
    - Inform individuals about the symptoms.
    - Raises the importance of CFS in the public's perspective.
    - Validates credible sources where people can seek information.

All campaign elements—including television and radio public service announcements (PSAs), print ads and other printed material, and the traveling photo exhibit—positioned CDC as the source for CFS information and drove traffic to access the CFS web page, www.cdc.gov/cfs.

The majority of resources spent on this awareness campaign has been on the pre-campaign material development, radio and TV PSAs, and paid advertising in mainstream journals (*Ladies Home Journal, People, Home and Garden*). There is about $900,000 remaining until September 2009. Given this modest budget, the focus at this point is not on paid advertising.

Samples of media coverage:

Earned media since the November 2007 CFSAC meeting mostly centered on the traveling photo exhibit in the Philadelphia area (print, radio talk shows, and television talk shows); the Lake County (Tampa, FL) area (print, radio, and TV); Phoenix (radio and TV). The exhibit also traveled to CDC headquarters in Atlanta for the month of December 2007 where it generated a lot of print and broadcast media. When the exhibit travels to a city, CFIDS generates interviews and articles about CFS to raise awareness.

CDC also coordinates with CFIDS on outreach to three or four major healthcare professional organizations around the country.

Upcoming photo exhibit venues in FY 2008:

- May 16-22: San Antonio Public Library
- May 24-29: American Academy of Physician Assistants (national conference)
- June 23-29: Maryland Science Center (Baltimore, MD)
- July 17-21: Great Lakes Mall (Mentor, OH)
- August 14-18: Penn Square (Oklahoma City, OK)
- September 22-29: Peyton Anderson Health Education Center; Medical Center of Central Georgia (Macon, GA)

Public Awareness Campaign focus areas (through September 2009):

CDC is discussing strategy with CFIDS to reinvigorate some of the activities that are currently part of the awareness campaign without major spending on paid media by—

- Recontacting TV and radio stations that previously used the PSA.
- Continuing the photo exhibit tour.
- Strategically distributing collateral materials developed by CFIDS that were not used in the original media launch (i.e., brochures, healthcare profession toolkits). We got agreement from the CDC research program that it would be appropriate to continue to distribute these materials.
- Exploring opportunities for cost-effective, paid online media (WebMD, Google Health).
- Continuing the trend in place since August 2007 of CDC Marketing and Communications working more closely with the research program. There is much more integration between research and provider education/public awareness due to Dr. Reeves' interest as well as the presence of a new health communications specialist who has joined the research program. She participates in the biweekly conference call between CDC and CFIDS. The Marketing and Communications staff has also benefited from a new member who came from CFS Public Awareness subcontractor Fleishman-Hillard, where she helped develop media materials for the campaign.
- Working with Dr. Reeves to develop an article for peer review based on DocStyles and HealthStyles data.

- Improving the DocStyles online survey during summer 2008.

Committee Discussion

Dr. Oleske opened the floor for committee members to question all three CDC speakers.

Ms. Artman: I've notice that on the CDC CFS website, under the categories of Treatment and of Diagnostic Tools, there is nothing on fatigue or on post-exertional malaise. There is nothing showing how to measure fatigue levels or how to advise patients on dealing with post-exertional malaise. What can be done to rectify this, if anything?

Dr. Reeves: This will not completely answer your question, but the United Kingdom National Health Service recognizes CFS/ME as a real illness and has initiated a national program. The health service's National Institute for Health and Clinical Excellence (NICE) has published UK-recognized and endorsed guidelines for evaluation, diagnosis, and treatment. Those guidelines are available on the CDC website. Additionally, the CDC physician focus groups understood that the SF36 multi-dimensional fatigue and symptom inventory can be useful for diagnosing and treating CFS, and we give out inventories for free. CDC is also collaborating with Dr. [Jose] Montoya [of Stanford University] to implement those instruments in his research team's studies of treating HHV-6 and to help evaluate their data.

Dr. Jason: I really like having 35 minutes where the committee can ask speakers follow-up questions, because it is critical for us to have a dialog with the people who made the presentations. I think this is the first time that I have heard Dr. Reeves say "CFS/ME" and I wonder if that signals a change in terminology for the disorder. More importantly, the committee had a discussion at the last meeting about the CFIDS Association's contract ending. What will the impact be on provider training? What are the reasons for ending the contract?

Dr Reeves: The NICE document addresses "CFS/ME" and that is why I used the term. With respect to CFIDS, CDC supported a contract that allowed us to develop the provider education components that largely led to the public awareness campaign. CDC is now endeavoring to make that work smoothly and to analyze it.

Kim McCleary [President and CEO of the CFIDS Association] discussed at the November 2007 CFSAC meeting why her group elected not to pursue continuation of a sole-source contract. That contract was outstanding and let us put together a dynamite provider education program. It took 11 percent of our budget to do that, but it was money well spent to get us where we are.

We have found that much of the original provider education components are not cost-effective. We are now maintaining the CME component of that and as I showed, both the number of hits and the completion rate have doubled. This is probably because providers—or anyone—take a website that ends in .gov more seriously than they take a website that ends in .org. There is a lot of research confirming that.

From our perspective, we are saving about half a million dollars a year which we believe can be used more effectively to look at the path of physiology, biomakers, and treatment for CFS. We are maintaining the website and jettisoning those provider education components that are not cost-effective. In my opinion, the impact of ending the CFIDS contract is that we have saved a substantial amount of money that will help us look for biomarkers rather than go to meetings and hand out brochures. We would not be here had we not had the contract. The CME access and completion rate have doubled. We know we don't need to go to meetings. We know that we need to provide CMEs. We know what the people are interested in. We know what is making an impact, and we're saving money.

Dr. Jason: Do you both feel that you have adequately responded to the five recommendations made by this CFSAC at its last meeting?

Dr. Reeves: I would point out that those are recommendations to the Secretary of Health and Human Services, not the CDC. As I have pointed out at multiple meetings, with respect to the research program, with respect to public awareness, we take this very seriously. I believe we have responded programmatically to the majority of suggestions when we can, but this committee exists to make recommendations to the Secretary of Health and Human Services, not to the Deputy Director of Science for CDC, the chief of the media campaign, or the principle investigators. Those recommendations have gone to the Secretary, not to us. We're on the committee, we hear them, and we do what we can.

Dr. Fridinger: CDC's presence on the Web is actually out of the National Center for Health Marketing. CDC.gov went through a major redesign a little less than a year ago, including the CFS pages. The research program made a request to oversee the website with our input, and I thought that was a very good idea. It probably is cost effective and certainly is much more efficient, because a lot of the updating of the website comes from the research program. It made sense to have their insight, and then we can modify as we see fit.

Dr. Miller: The recommendations, from the standpoint of the Office of the Director of the National Center, are the heartbeat of this committee. They show what you are seriously interested in. One of those recommendations was that CFS oversight be at the Director level. Well, it is certainly at the CCID Director level with Dr. Cohen, but they do not do program at the Coordinating Center level. We do that at the National Center level, and we are fully engaged in CFS. CFS does have a home, and it is very important to us. One of the recommendations was to find a home for the CFS program, and it does now officially have a home in our national center.

The recommendation was to expand the research to include behavior, etc., and I think I showed you the list of skill sets. Dr. Reeves has also presented a number of times on the broad skill sets that are available and released into the CFS research program.

I think that one of the recommendations was to expand external collaborations, and you saw the list of external groups that we are now collaborating with. Granted, that may not be everything you would like to see, but we have to work up to that. We only have a certain

number of resources to work with. If we could hire ten more people, we literally have no place to put them.

So, we are doing everything we can to accommodate the observations and the wishes of this committee. If we can answer in more detail, we'll do it in a heartbeat, especially if a request comes through CFSAC to Ms. Wiley or to me or to Dr. Reeves. If your recommendations are not fully addressed, then we need to work on that, but I think that we have gone a long way towards addressing them.

Dr. Jason: I really appreciate you coming back to those recommendations because I think that is the guts of what our process is about—us making recommendations and having a chance to talk to you. I'm hoping to maybe go through some of the recommendations specifically and talk in more detail. I also want to get onto another issue, and that is the blue ribbon panel that met in January 2007. There were some reports that came out of that group. We've never had access to those. Is that information available to us?

Dr. Miller: That blue ribbon panel report has been completed. It was through the Coordinating Center for Infectious Diseases. It should be available. I will find out for you what the status is.

Dr. Jason: We really appreciate that you are introducing a new blue ribbon panel and that you are asking us for input about potential members. It is also just as important from our point of view to make sure that we understand what happened at the prior one.

Dr. Miller: This new body that I mentioned is not a blue ribbon panel. It is actually an external peer review of the program, which will be even more robust and more directed by those experts.

Dr. Jason: I am the chair of the CFSAC research subcommittee. I and members of my subcommittee have been most interested in understanding how funds have been allocated at NIH and CDC over the last number of years. There has been information that has been provided. However, in my efforts to get information on specific funding and how the funding occurred—particularly at the CDC—when I have asked Dr. Reeves this for the record several times, he has suggested that if I want that information I should issue a Freedom of Information Act request. I have not done that. That's not something I intend on doing. So I was appreciative of the fact that you mentioned that information about funding at the CDC for the last few years could be made available to our subcommittee. I just want to make sure that this is accurate and that we will be provided this information.

Dr. Reeves: I advised that CFSAC must request this information from the Director of CDC, not that Dr. Jason should file a Freedom of Information Act request. This is an official committee. If this committee requests that information through the appropriate channels at CDC, CDC will provide that information. That is not a Freedom of Information Act request, that is also not Dr. Jason specifically requesting it, it is this combined committee requesting that information from the Center for Disease Control and Prevention.

Dr. Papernik: Regarding Rebecca's comments, I'm not sure that it was in the purview of the CDC to put down every treatment that's available for CFS, because then it's sort of taking over what the patient's primary doctor should be doing. I think any governmental website that gives information about disease states really should be giving generalized information instead of specifically saying, "You should be doing this; you should be doing that," because that is serving the physician's role.

Secondly, I agree that the illness and its impacts in patients is paramount, but I think that body count is also important due to the fact that it can sometimes demonstrate the impact on the economy as a whole to a greater extent than just looking at individual patients. I think that we shouldn't discount the fact that we need good epidemiological data to show the body counts of how many patients have CFS because that impacts on our ability as a committee and as a society as a whole to get more money and more research being done for patients with this illness.

Dr. Reeves: I can't take complete exception to that. What we are trying to do with respect to the body count in Georgia—where we have very good statistics on how long people have been ill, what proportion have seen a provider, what proportion have had this diagnosed and treated, physicians' own KAB—is to reduce the morbidity. I will have measurable outcomes if I can get 60 percent of CFS patients to see a provider; if I can say that with this kind of education and that kind of facility, 20 percent of CFS patients become diagnosed and treated, 60 percent of providers are diagnosing it, and fewer of them have questions about how to diagnose it and treat it.

The 4 million number is a tricky number. Dr. Jason would say 1 million, and it's somewhere in that range. I may never show a decrease in that overall number in the U.S., but I can show some very measurable decreases in a place like Georgia. I can show differences in lost earnings and wages and I can show differences in provider costs. With that information, I can potentially convince HMOs or insurance companies to cover the treatments. I can actually show changes in morbidity, which is what is behind the importance of the body count. The economy of CFS is important because that is where decisions are driven from.

Dr. Hartz: The CDC has a major emphasis on provider education, and I wanted to find out how you would characterize what the major problem is with how providers deliver care. What is it that is missing that you want to try to address?

Dr Reeves: We don't really have direct information on that. That's one of the things we will get direct information on from the provider registry. But what the data would show is that providers would say, "We don't really have a good idea how to diagnose and treat CFS." Increasing such information in toolkits and provider education would address that. I do not have data on specific providers because I have not yet been able to directly target them.

Dr. Hartz: Do you think it's known how providers should be managing these patients and they're just not doing it the way it's known to be effective, or is the problem even before that?

Dr. Reeves: We really don't know on a population basis how they are treating it. The evidence base would be that occupational therapy, graded exercise therapy, and cognitive behavioral therapy are those therapies that have been shown to be efficacious on a population basis. There are other things coming down the pike. Will some of the anti-herpes treatments be replicated and be done in very rigorous studies? I do not know. Will some of the searches for the pathophysiology and some of the modeling give an indication of potential drug targets? I do not know. We're poised to do that. But right now the evidence base is the therapies I mentioned and managing the symptoms.

Dr. Hartz: Can primary care physicians really manage or provide those kinds of treatments?

Dr. Reeves: I think there's some controversy about that, but we're certainly targeting primary care providers, family care practitioners, and OB-GYNs.

Dr. Hartz: So your goal is to teach them to effectively use those particular therapies in their practice?

Dr. Reeves: That is correct.

Dr. Snell: It seems to me that this peer review panel is going to be an important milestone in CFS research and I'm pleased to hear that we'll have some input into the people who may be on that panel. I wonder if you could give us more information about the process, the context for the review, timelines, the sort of areas that they're going to be looking at, and the reporting procedures.

Dr. Miller: I want to make one more comment on the budget issues. You now have a direct communication link for budget items. Please make a request to our Center through Sarah and we can get that information for you from our financial management office at the high levels where that money is tracked.

In terms of peer review—external peer reviews are usually held at CDC over a two to two-and-a-half day period. During the review, a specific component of a program is evaluated in detail. In this case, the specific component would be the CFS program. It may be just the laboratory component that is evaluated, or it may be a broad range that would include education and marketing. That has not been decided yet, but it will be the CFS program.

The panel will be external experts in the field who have no conflict of interest—they are not receiving CDC funding and would not have a direct impact on the program in its development in stages other than the recommendations. These people would receive a series of presentations as well as a notebook filled with information about specific research agendas, budget items, etc. that lay the CFS program out on the table. There will be a charge to the committee from the director of that peer review, which might be the director of a division or center. The charge will specifically state what CDC wants the review to accomplish.

We want a review of what we're doing about CFS, things that we should be doing that we are not doing, things that we're doing that we should not be doing, etc. There may be roadblocks

that would keep us from doing what needs to be done. The expert panel could help us remove these blocks before we ever get to them. There will be a series of questions that the panel will answer in a final report that includes recommendations. This report will be broadly available meeting.

It's going to be a win-win situation for all of us, particularly our science, and our marketing campaigns. We will be able to get direction from those on the outside and mesh it with what our own goals and strategic plans are. We will have more ammunition to develop a strategic view of a research agenda that we could move forward with. Not everything recommended by the reviewers may be accomplished, but we would certainly hear from the experts to help us make those plans.

Dr. Snell: It is not clear to me whether it's going to be a complete program review, or selected aspects of the program.

Dr. Miller: We have not gotten that far in the planning yet. We haven't talked to Fred and his group. He may want to be a part of this review. But as we get to the scientific component of this, it may turn out that it's going to take two-and-a-half days just to review that component. We will have to make that decision internally and draw up the plans for the review.

Dr. Reeves: We've had two peer reviews of the CFS program, but they've been some time ago. They were actually when the program was quite simple. What we have—and it's difficult for peer reviewers—is a sophisticated clinical laboratory component that is getting at biomarkers, pathophysiology, and mathematical modeling. We have control and marketing aspects, which we really didn't have before. It has become quite a complex program to review. Does one want to look at the laboratory component, the control component, or all of it? The previous reviews have been terribly helpful. They made a huge difference.

Dr. Miller: Let me request that CFSAC submit to us some recommendations on some things that you would like to see included in the peer review keeping in mind that we are constrained by time. We can take it under advisement as we make our plans to try to accommodate your wishes.

Dr. Oleske: I can call on my experience with HIV/AIDS, particularly in the beginning when we developed treatment guidelines before a virus was isolated. We know that CFS is a fairly complicated disease having metabolic components. There may be some infectious disease components, there's probably multiple causality with a number of organ systems and the immune and endocrine systems involved. I want to let people learn from my mistakes. In the beginning we really thought that we could know enough about HIV/AIDS to get every primary care doctor out there taking care of patients. That never worked, and as it turns out, it was destined not to work. I want to put that caution out.

As far as the CDC and your mission, you don't have anybody who respects the CDC more than I. The only people who gave me funding at the beginning of the AIDS epidemic in 1983 was the CDC. I'm just concerned that as the CDC embarks on its CFS mission, it includes its sister agencies. AHRQ and the NIH have an interest in making sure that guidelines get out

there to the right people. The NIH does research and the CDC does public health/disease research, which I respect tremendously. But this disease is very complicated. I would hope that the agencies come together when any one of them is launching a massive campaign to approach this disease and recognize that the sister agencies need to be onboard and be participants. We need to break down some of the walls that get built up, because we're all competing for precious dollars.

I think that the patients deserve agencies that become wise about expending the resources on the answers to questions that most impact patients' lives. With HIV, we started treatment trials before we knew what it was. We can also do that with CFS and that model, I think, is very important. While we're waiting, we should try to evaluate available treatments that if not curative, improve patients' quality of life.

Our questions may be harsh sometimes, but that's because we feel the pressure of the patients saying, "What is being done about this disease?" There are a lot of Americans who have CFS, just as there were lots of Americans who had HIV, who are concerned and upset and want to be cared for. I think that we have to reflect that urgency in our questions. We support the work that all the agencies are doing.

I have one request—please let's not use that term "body count." I think that it's offensive. It's patients, it's people who are ill, it's the ones we have to serve and care for. My son was in Iraq and I know what a body count is, and I don't want to hear it about patients who we're taking care of.

If you could, please respond to my question about the sister agencies and coming together with these internal reviews.

Dr. Miller: We want to work with everyone we can. Bill has certainly worked with the Department of Defense and a number of other sister agencies and we do not plan to stop doing that. I think that with the campaigns you heard about today, that will be a given.

Ms. Healy: Can you update us on what's going on in Macon? You said that there might be a workshop this spring that might begin to address people involved in that project regarding clinical interventions.

Dr. Reeves: We have planned a provider registry in Macon. The registry is awaiting Office of Management and Budget (OMB) clearance before it can be launched. If the registry is approved without questions and does not need to be revised, we will have a kickoff that will be a town hall meeting of providers and the public. We are trying to do that in June 2008. We've already had focus groups. Right now we have a fully staffed clinic in Macon that we're using for our in-patient study.

Ms. Healy: How will the clinical intervention side of things work?

Dr. Reeves: Right now that's in the thought process stage. We want to find out exactly what providers are doing there. There's a medical school in Macon that is interested in

collaborating with us. I've had meetings with the medical society—they're extremely interested in collaborating with us. Emory is interested in a joint teaching program with that medical school. Our thought is to use the clinic that we have in Macon as a training center and as a center in which one might be able to do some intervention trials. The kickoff of the registry just requires final OMB approval.

Ms. Healy: It would be very helpful to have those kinds of research questions addressed at the facility so that maybe we could have some more up-to-date evidence-based guidelines for clinical interventions in the future. Maybe this committee could speak to that as a whole later on.

Mr. Newfield: My concern is that we're here twice a year, we have a burst of activity, and then subcommittee meetings in between. I'm wondering whether budget information can be provided very quickly so that we can incorporate it into our dialog in the next day and a half and use it for further recommendations. I think that it's critical that the information be provided while we're here rather than in between.

Mr. Miller: I can say that if you ask us through the communication channel that we've opened, you will have a much faster response. I can't tell you that our FMO will be able to give everything you expect. Sarah will be the one who can coordinate that activity and can provide just about everything you need much more quickly.

Ms. Wiley: As far as getting it in the next day and a half, I can't promise that, but I can promise that I will try. I need to know what the questions are.

Dr. Oleske requested that Ms. Wiley meet with the Research Subcommittee during the CFSAC subcommittee breakout session and she agreed to do so.

Ms. Artman: Are the awareness campaign toolkits still being printed? I found them highly useful and probably placed a case myself directly into different doctors' hands. It was effective for me to be able to give them something with the CDC logo. When I just told people about going to the CDC website, there was no follow up. But when handed them a toolkit, I found that when I then went back for a return appointment, they had used that toolkit and had visited the website.

Dr. Reeves: We have the toolkit printed up and if a request is made, we can certainly provide those. Just send the requests to me.

Dr. Jason: There are guidelines being developed by the International Association for CFS/ME (IACFS/ME). Nancy Klimas is overseeing that. For the record, hopefully we can make presentations on that at the next meeting. There are about seven to nine different topics that guidelines are being developed for.

My second comment has to do with the issue of funding. I think that you can understand why it's important for us to have this information. If we are the committee that's trying to make

recommendations to the Secretary of HHS, we need to really have information concerning how funds are being used by the Federal government, particularly CDC and NIH.

I have a question for Dr. Reeves. What one calls this illness to define it and how one measures it is critical to any scientific work that's done in the field. The case definition and what we call that case definition are fundamental issues. There is a large debate going on about whether we should transition from the term CFS, which most patients feel is somewhat trivializing, to something that's more medical sounding. CFS/ME is one possibility. There are interest, scientific, and patient groups and organizations that have begun to use the term ME/CFS. When I heard Bill Reeves mention the term in reference to the NICE guidelines, I wanted to ask both Fred and Bill—is there some discussion in your offices about using the term CFS/ME or ME/CFS? If there is, what's that discussion about? And if there's not discussion, is it considered an issue that doesn't have scientific merit?

Dr. Reeves: We're trying to control the illness and identify biomarkers and the pathophysiology. That's our main emphasis. Devoting a large amount of effort to dealing with the name dilutes from that. I think that one needs to consider that 90 percent of providers know about CFS. Based on my experience with hepatitis/HIV, it introduces a large amount of confusion into the field when marketing and education campaigns have been based on a name, people understand it, and then it's changed for no valid reason. The term ME/CFS has been used historically in the UK. We just believe that there are more important issues to deal with in the research program and we believe that there is the possibility that you will send very mixed messages and you can dilute much of the education campaign by changing it.

Dr. Fridinger: This was raised previously, and I think my comment at that time, from a marketing perspective, was similar to Dr. Reeves. In the case of the public and their perception of this disease, they're aware of CFS and calling it by another term might create confusion and mixed messages. I think that is possible. As a project officer, I consider that we've already got materials based on one name. If we change it, there are costs associated with that. From a social marketing perspective, I've always incorporated the saying, "the consumer is always right." Whether they actually are is somewhat irrelevant. It's what their perception is, what they think. If consumers are pushing for the term ME/CFS that would certainly be something to take account of, and you would want to consider making some changes. But determining that would require some formative research.

Dr. Jason: There actually has been some research on names and their affects on attributions that may be worth taking a look at. If over 90 percent of patients affected by this illness want the name changed, how would you respond to the fact that there's not effort being made to change the name in your office?

Dr. Fridinger: I think that we would have to look at that.

Dr. Reeves: I would want to be shown that 90 percent of patients in fact thought that, and not 90 percent of a particular organization. It's very easy to say that every person with CFS feels

that the name is demeaning. This may or may not be true, or may be reflecting one's own opinion.

Dr. Oleske: This is really a research question. If it's a question of what percentage of patients feel differently about the names given to an illness, it may be worth looking at the literature and research that's been done, or maybe even do some more work in the area. Just as important as what we call this illness is how we measure it. It's like a house of cards. The bottom set of cards is the case definition. If that house has problems with specificity and sensitivity in using epidemiological terms, then all types of work that occur can be compromised.

There have been issues brought up with the new case definition as well as the research that's going on in Georgia. When you published that case definition, one of the reviewers—Peter White—questioned your inclusion of the SF36, particularly the emotional health issues, as one of the criterion of disability. If an individual indicated that he/she was having some emotional difficulties, he/she would hit the disability criterion. Have you considered White's critique as well as other professionals' critique of the case definition? In your response to him, you indicated that you were not going to change that case definition. Have you thought any more about his criticism as well as the criticism of that issue from several other scientists?

Dr. Reeves: What we have tried to do is follow the recommendations of the International CFS Working Group, of which you and Dr. White were members. That group published recommendations under the authors' names that said that the SF36 was at that time the best instrument to use to measure overall disability. So we followed the recommendations of that group. Is that the single best instrument in the world? I don't know. It's an instrument whose properties are very well known and can be reproduced. And so we have a biomarker—something of which we can actually say, this is the gold standard. Those were the final terms. We are now using those. Other serious investigators are using those same instruments. We certainly talked to Peter White about this way before he wrote his article. We talk to Dr. White fairly regularly.

[Dr. Oleske called a five minute break.]

CFSAC members divided into the Education, Research, and Quality of Life Subcommittees for their scheduled morning meetings, which continued through lunch.

Dr. Oleske amended the agenda format that called for three 30-minute CFSAC subcommittee presentation/discussions. He called instead for three five-minute presentations in which each Chair summarized his/her panel's discussions. These summaries were followed by a question/discussion period, which Dr. Oleske said would accommodate and encourage the natural interaction between subcommittee members and the overlap of their topics.

Dr. Parekh noted that Dr. Reeves' presentation was available to members of the public and had been distributed to all CFSAC members. He added that there was an additional public comment available to the public and to CFSAC members.

Subcommittee Updates

Dr. Leonard Jason (Chair) reported for the Research Subcommittee

We are grateful that we'll be getting information on the primary issue of funding. We'll be able to see exactly where allocated resources are going at both the CDC and NIH.

- One thing that we think is important is Requests for Applications (RFAs) at NIH. When an RFA came out at NIH concerning CFS, there was a spike in applications and, particularly, grants that got funded. There were at least six grant applications that were funded. It seems that RFAs galvanize interest in applications and ultimately funded projects.

- We are in discussion with Dr. Hanna on a potential workshop in the future concerning treatment approaches for illness. As you know, workshops sometimes lead to RFAs.

- Our group continues to look at information in medical textbooks concerning the training of the next generation of individuals who will treat those who have CFS. I will be able to report more about this in six months but for now, we looked at approximately 130 textbooks and found that approximately 43 of them had some mention of ME/CFS. Unfortunately, less than .1 percent of content in those textbooks was devoted to the subject. In terms of emphasis in those textbooks, if you look at etiology, the emphasis is on psychogenic explanations. Treatment approaches tend to be somewhat narrow. Nothing is said about alternative medicine, for example. We'll hopefully have a final report that we'll be able to issue to the committee at the next meeting. This might be a basis for taking some action to get more content as well as appropriate information to our healthcare professionals who are being trained.

- Finally and most importantly, we had a meeting with Dr. [Cheryl] Kitt [Deputy Director, Center for Scientific Review, NIH] by telephone and she was very amenable to having a dialog with us about using the CFS Special Emphasis Panel (SEP) to pilot new ways of doing reviews. She will be here tomorrow afternoon. Our research subcommittee is going to be requesting the following types of specific mechanisms for piloting:

    1. Allow researchers to give the names of potential reviewers from which the Scientific Review Officer (SRO) could select. As you know, SRO Terry Hoffeld will be retiring and a new person will be taking over, so it's a good time for us to be presenting giving CSR ideas.

2. A list of experts compiled by CFSAC in conjunction with other scientific organizations that we present to the SRO so that he/she has people who have expertise in CFS to do reviews.

3. A two-tier system where the PI has a multi-disciplinary group of qualified reviewers examine the proposal and determine whether it's fundable. Those proposals that get into the top 50 percent would go on to a formal review. CFSAC would recommend that people who are submitting grant applications also give feedback about their review experiences. After removing names and other details to maintain anonymity, this information would be available to CFSAC so that we can be constantly reviewing how successful these changes are.

Dr. Glaser: The comments on pages 30-31 of the November 2007 CFSAC meeting minutes reflect how those of us on the Research Subcommittee feel about the review process, the SEP, and the hurdles that were just out of line with a fair review process. We calculated that about 15 percent of the members of three different versions of that study section had anything to do with CFS. The minutes present a fair summary of the concerns that we had on that. We have an opportunity to use the SEP as an experimental study section to try out some new ideas and I hope that Dr. Kitt will listen to some of this.

When researchers send a paper to a journal, we are often asked to submit the names of four reviewers. If we can do that, why can't we do the same with a study section? We can take into account conflict of interest, as do the journals. Then if the grant doesn't get funded, you've still had the best chance in terms of a fair review.

We want to try to make it attractive for people to continue to stay in the field. If you don't feel like you're getting a fair shake after all the work it takes to write three grant proposals, you're more than likely not going to stay in the field. Making the review appropriate and having people with the right backgrounds review grants, will help the credibility of the review side of the CFS field.

Ms. Kristine Healy (Chair) reported for the Education Subcommittee

The subcommittee continued since the November 2007 CFSAC meeting to work on the Surgeon General (SG) letter, submitting some additional recommendations on what organizations should receive the letter and some concepts on how outcomes might be measured.

Unfortunately, we've learned this past week that the SG is not able to engage at this time in disseminating our letter to providers. My understanding is that tomorrow a representative from the SG's office will be here to discuss that with us.

Our Education Subcommittee is considering other avenues for future recommendations. For example, is there an opportunity to have advanced provider education in CFS—maybe a CME-type model, which is knowledge-based—but also an opportunity for training in concert

with some of the research efforts that are going on at CDC? This would allow clinicians to gain expertise and confidence in the care of patients with CFS. We are examining the possibility of creating a model for provider education in the future.

Mr. Jason Newfield reported for the Supportive Care/Quality of Life Subcommittee

Given the first presentation today discussing the creation of a CDC external review panel with CFSAC input, we put that to the forefront and felt that it's the most important focus for us. We identified substantive areas that we want to open up to the entire committee.

We think that this is a great opportunity for CFSAC to influence a process in which we can be significant participants. We want to discuss not only the areas that the external panel should be focused on, but the names of participants. We identified a number of names, but we'd like to open it up to the whole committee to nominate potential review participants.

We also keep coming back to ongoing themes:

- Our desire for standardized diagnostic tools and/or a case definition that will allow practitioners to reach a diagnosis. We ask that Dr. Snell speak about his work on this.

- That dovetails with the need for there to be more doctors on the front line to be able to provide patient care. We need to fill the void left when current practitioners retire by influencing others to get into the CFS field.

- This comes back to the Centers of Excellence, which is the drum that has been beat and beat again, but we feel that it's critical, and we're going to continue to beat that drum. We need new practitioners to enter this field to help our patient population.

- The last theme is life issues and potential for return to work of the population of CFS patients who are finding some recovery or are in remission.

Dr. Snell: The results of my research on diagnostics will be available to everyone when I publish it for peer review. One area that I think people need to look at when diagnosing and assessing CFS is functional capacity. Practitioners need to be able to actually assess the fatigue that is the defining characteristic of the illness. We feel that that's an important characteristic. Sometimes practitioners can go through the diagnostic list without doing any functional assessment at all and rely instead on patient self-reporting. I agree with Bill that the SF36 is extremely good at distinguishing CFS from other illnesses, but once again, it's a self-report instrument and must be looked at in conjunction with other assessments. There are already functional assessments out there that can be applied to this illness.

Mr. Newfield: In the work that I do, I see a lot of defective functional capacity tests that have individuals participate in a minimal series of strength, endurance, and various other activities. Those results often get extrapolated and/or used against claimants based upon their limiting behavior. I've had discussions with providers who actually do some of the things that you do, Chris, with regard to measuring the post-exertional malaise. I think it's critical to have better

testing that really does address post-exertional malaise rather than measure the patient's ability to participate in two or three hours of activity with no assessment of what the post-exertional effects are. I think that that's a void that needs to be filled.

Committee Discussion

Dr. Oleske: When CFSAC members break into subcommittees, we are sometimes isolated into three separate camps and we're not as effective. It was Dr. Parekh's idea that we hear three subcommittee presentations, then have discussion that fleshes out all of the ideas so we can give more unified recommendations from CSFAC as a whole.

This morning when I talked about my experiences with HIV, it got me thinking about how we built up the cadre of physicians who would care for HIV patients. In the beginning, there were a lot of doctors who refused to care for these patients. Then there were a lot of doctors who were generalists who acquired significant expertise through caring for many HIV patients and were dedicated to doing that. There was a debate over whether you had to be trained in infectious diseases in order to treat HIV or could acquire some special expertise through treating the disease. We answered the practitioner shortage by:

- Starting HIVMA, which was a group whose members took care of at least 20 patients with HIV and were willing to see other patients?
- Developing a straightforward certification exam.
- Allowing any care provider—nurse, doctor, social worker—to join our group and be certified. It didn't matter whether they had a residency in infectious diseases or immunology.

One of the things that I think might come out of our subcommittees is improving the number of people taking care of individuals with CFS and not losing anybody over time. Let's recognize them and form some type of group. I don't think that we can recommend that to the Secretary, but I think that we can, as a group, say that we need to do this independent of our work here. It is a way to maintain the pool of physicians, nurses, and social workers who care for CFS patients. The members of such a group could pool patients from around the country for studies, trials, and diagnostic tests.

I just want to throw that out as a starter on an open discussion of how we're going to take our three subcommittees and come up with recommendations that are heard—not accepted without debate or discussion, but at least listened to.

I want to thank the CDC for the showing we had today of people who knew what we recommended and responded to it in ways that gave us some real insights about how we can work with the CDC in furthering its goals of providing leadership in the epidemiology and eventually the care of CFS patients.

Dr. Jason: I want to thank you and Anand for opening up the discussion. This has been a very helpful meeting. We have asked for that and I know that you both have been very responsive to giving us more chance to dialog on these issues.

Christopher mentioned post-exertional malaise as being a critical issue for us to be thinking about. I find it interesting that in the case definition that we currently use, you can be diagnosed as having CFS without having post-exertional malaise. Under the Fukuda criteria, you need not have short-term or long-term cognitive problems, unrefreshing sleep, or post-exertional malaise, and you can still be diagnosed with CFS. That's a challenge for us when we have cardinal symptoms that are not being represented. The Canadian case definition, as well as the pediatric one that the IACFS/ME has been working on, do make these particular symptoms critical.

In terms of your idea, Jim, I that think the IACFS/ME might very well like to work with you on this initiative. Nancy Klimas, as you know, is the president of this organization and there are several board people on CFSAC, including myself. I would strongly urge us, and you Jim, to continue this dialog with Nancy because I could see this as a really important service that our organization can provide. If you have particular energy and interest to work on this, that would be fantastic.

However, I must mention that as much as we want to certify people in the area, one of the greater needs is getting people who are interested in CFS to be available. I know with the loss of Morris Papernik in the Chicago area, I get phone calls regularly saying, "Who can treat me?" How do we get more people interesting and willing to be in this field?

That leads me to something that Jason brought up—the Centers of Excellence. In Reno, there's going to be one of these types of Centers of Excellence. CFSAC has constantly said that we need centers that are available for patient care, research, and ultimately the training of the next generation of medical personnel. I just want to keep emphasizing that we have made that recommendation. Now how do we take the next step on that? I'm not sure what the next step is, but I hope that we, across the three subcommittees, can continue to dialog on that. This has got to be of central importance to our group.

Dr. Oleske: I think that having a way of certifying people attracts people to the field. People want to have a badge of courage and recognition. But I agree with you on the Centers of Excellence. We have gone on record since this committee has been in existence.

Ms. Artman: Would it be feasible for us to brainstorm some ways that we can bring people into this field? A lot of physicians who are leading experts are starting to retire and we're not seeing a resurgence of new people coming in to take their place. When my doctor retires, probably within the next three years, I will have no one in the state of Florida who is an expert in CFS. I can go to my family practitioner who has been educated with the CFS toolkit, but he does not want to treat the illness. He wants to be aware of the illness, but he does not want to treat me for any of the symptoms involved with that illness. He wants me to see a specialist. This creates a complexity for every patient who is in this room.

How do you find a physician? How to we bring people into the field to treat patients and also to research the illness? We've talked about special RFAs and Ken Friedman is going to talk about the New Jersey Association offering a scholarship, but I would like to see us really

brainstorm how to bring new healthcare practitioners into this field. We have to come up with some solutions and then make recommendations. We can't just keep saying, "We need a Center of Excellence." We're being told that it's not going to happen, so now what do we do? No matter what, we need physicians to treat this illness.

Dr. Bateman: On the Education Subcommittee we spent about half our time talking about the need for more medical providers. We're all clear that the majority of medical providers now understand that this is a real illness. Only 30 percent of the providers surveyed felt that they had enough information to make a diagnosis. There's still a perception that there's nothing that can be done to treat CFS. We do definitely need to increase the confidence and the skill of those medical providers throughout the country so that ordinary patients can get a diagnosis and good care whether it's on the primary care level or whether we develop some kind of a network that allows people to be more well trained in a specialty way.

Dr. Jason: Could you review for us and for the people who are in the audience what has been the history of the recommendations for Centers of Excellence? Jim, can you give us a review of what the roadblocks are and whether there might be creative ways around these roadblocks?

Dr. Papernik: This issue with the Centers of Excellence, I think, is that it's too broad and it's too big. If we're going to develop something like that, I think we need to think on a smaller scale that is more easily managed by whichever government department is appropriate. The Education Subcommittee talked about an alternative to setting up five different Centers of Excellence throughout the country, which would cost quite a lot of money. We were looking at one centralized area that would be the core of information gathering. That core would be connected to several of the specialists throughout the country who deal with CFS. Information would be fed into and filed at this one centralized office. In that way we can develop outcome data and we can develop a lot of evidence-based issues.

That always seems to be the problem with this illness. People want to have evidence-based medicine; people want outcome data and we don't have it to give. Instead of thinking of large-scale Centers of Excellence throughout the country, we discussed a smaller-scale, office-based core that is connected to other offices through an electronic medical record system. It would be a more amendable request compared to asking for five Centers of Excellence.

Dr. Oleske: I don't know what we can afford or cannot afford. Looking at budgets and the debate that's going on in this country now with the political campaigns, there appears to be a lot of money that we can spend if we want to spend it. From our perspective, healthcare has never been adequate to the needs. We know that prenatal care is the single most important factor for healthy babies, and yet in some cities in the United States, 20 percent of the women don't get prenatal care.

The challenge of how we retool our finances so that we pay for the more pressing health needs and not for the things that are the antithesis of health—war, killing, slaughter, bombs—

is an issue. Possibly as we go through this electoral process, we can do some of that thinking.

As far as the history goes on the Centers, I would argue that it's sort of like which came first, the chicken or the egg. We argue the need all the time and it never happens. I would recommend that we still push for recognition that there are sites in the country that have a long-standing expertise in CFS. It makes sense that if they have large populations that they've identified—whether it's in Chicago or Atlanta or elsewhere—there are ways to have four or five Centers of Excellence.

There's always a problem of self-interest. The Federal government—the NIH and CDC—has to be very careful that it doesn't look like it's caving into self interest. The thing that bothers me is that there aren't a lot of people who have expertise in CFS, and most of those people are advising the government and applying for funding. You immediately get questions of conflict of interest. What happens, then, is people get turned down and they don't bother any more because it's not worth putting effort and time into grants that are not funded.

It seems to me that someone at a higher level than CFSAC has to take up the cause of funding Centers of Excellence around the country. I would make a plea as a pediatrician that we do include adolescents and children because I do think there's nothing purer than a child. Sometimes if a child does manifest CFS—although it may be rare—you're not going to have many of the confounding variables that you have in adults. That's why pediatric AIDS was so important. We learned so much from it because children weren't 44 year olds who had already acquired hepatitis B and other diseases.

I think we could make a legitimate argument that there needs to be Centers if we're going to answer the questions about diagnosing CFS, finding an etiology, and short of that, treating symptoms to make people's quality of life better while we're waiting for the science.

The other problem with CFS is that it may be multi-factoral, and it's probably incited by both a genetic predisposition and events that can trigger it. When there's more than one specific inciting event in a genetic disease expression, it becomes difficult for people to recognize this as an individual specific disease that can be given a name and that a patient can be specifically diagnosed with. Right now, we sort of diagnose populations—large groups of patients that we see who may or may not have CFS. Many of them do have CFS, but then they have different etiologies, and that becomes confusing.

Centers of Excellence concentrate the abilities of known investigators with proven track records who can do the kind of basic science that will answer the questions. They collaborate with the CDC and the NIH. As a committee, we must keep pushing that idea until something happens because until there is recognition of the need for Centers, I don't think we'll get the kind of research that gives us a diagnosis of this disease and then an etiology.

In the meantime, for the patients' sake, there is a lot of symptomatic care we can give. I'm doing a year's sabbatical on end-of-life and palliative care in children. I can tell you that the reason I'm doing it is because the adult hospice model doesn't fit kids. The new model, I

hope, for children with chronic diseases is to do both therapies and symptomatic care. You may not know exactly how to treat disease and you may not have the perfect therapies, but you can address pain, fatigue, some of the other symptoms. You can also look at disease collaboratively and compare your work.

From Ampligen to rehabilitative medicine, until we have scientific proof, no insurance company will pay for appropriate rehabilitative care much less the primary care doctor doing the referral.

In answer to your question, Leonard, it's complicated. I still think we need to stick to our guns that we need to develop a core of people who can capture data in a scientific way that proves that whether CFS is multi-factoral or not, there is a way of diagnosing patients. Too many of us have done it for long enough and have the expertise to know that this is not a non-disease. This is a real disease that affects an awful lot of people and makes their lives very miserable. We should do a better job of insisting that we provide some care and treatment for these patients. That takes clinical trial groups. Until that happens, I think that you're all going to be out there doing what you think is best and not really sure that what you're doing is all good or all bad.

Dr. Jason: Jim, I agree with you that the fact that we bring this up frequently is probably a good thing. It keeps this as an agenda item. When one applies for an individual grant, the review committees often want you to specify one particular thing that's bringing about the change. In a clinical treatment center that's also a research center, you can look at multiple things that might be occurring, and that is why these types of centers are so important. It's a different type of research that is not looking at one solitary issue and is sometimes harder to get through a review committee. You need a treatment team that's working in the best interest of the patients.

I think we're all saying that it's important. The question is how do we get it into the field? You could probably talk about dozens if not hundreds of fields in which there are centers. Why is it that other illnesses that are less prevalent than CFS have centers and we don't? I think maybe we need to tap the expertise of some of the *ex officio* officers here who might know other ways of thinking about this. The reality is, at the NIH, translational research is something that people are really interested in. Difficult-to-treat, multi-systemic illness is what people want to understand. We have been exemplar in presenting CFS as an illness that needs centers. How do we get there?

Ms. Artman: Would there be any success in having something from the Secretary sent to every president of a medical school stating the CDC's statistics that 70-90 percent of this population goes undiagnosed, that 1-4 million people have this illness, that we need physicians in this field, and that we would ask for their encouragement of their students and staff in looking at CFS as a field that they would at least consider investigating? Is that a realistic thing to ask?

Dr. Bateman: I don't know if it's realistic to ask, but it would be great to ask.

Ms. Artman: Anand, is this something realistic?

Dr. Parekh: There are about 150-160 U.S. medical schools. I don't know the answer to that question. It's certainly within the committee's prerogative to discuss and recommend, but I don't know whether that's feasible.

Mr. Newfield: At the last meeting, I was looking over the minutes and I recalled that I had mentioned how nice it would be for Secretary Leavitt to appear. Is that something that is possible? I know that when we had Dr. [John] Agwunobi, he made a commitment to us to be at one out of every two meetings. He's no longer with us, and we have you at every meeting which is wonderful. I was just wondering whether Secretary Leavitt might be able to participate in any way.

To go further with what Lenny was saying, I started my presentation talking about the opportunity that we have with regard to this CDC external review panel. I think that we should spend the time brainstorming about what we're looking to influence that external panel about, perhaps broadening the discussion to include Centers of Excellence or a centralized facility. In the next day and a half, we need to recommend and/or create an influence over this external panel in order to further these clinical, research, and education issues. I think that's the most important topic that we should focus on.

Dr. Parekh: I will extend the invitation to Secretary Leavitt once again and certainly if not him, then the Assistant Secretary for Health. I do recall having this conversation with you six months ago, and nobody was able to come to this meeting, but I will certainly extend that invitation again.

In terms of your second point, I think that's absolutely what the committee should focus on right now in the time remaining before the next presentation. The CDC has asked this committee to provide input to the work that they want to do this fall.

Dr. Snell: I just want to concur with that. If anything, the CDC efforts in CFS are the closest thing we have to a Center of Excellence at the moment. It's a multi-dimensional approach with professional people looking at the illness. A review of those issues would be pertinent to making recommendations about how that might translate into other Centers that could continue the fight.

Mr. Newfield gave the names of professionals chosen by the Supportive Care/Quality of Life Subcommittee as worthy candidates to serve on the CDC's fall peer review of the CFS program. These included Drs. Anthony Komaroff, David Bell, and Ken Friedman. CFSAC members expressed the desire to nominate candidates from their own rank but were concerned that serving on the review panel would be a conflict of interest. **Dr. Parekh** said that he would look into the matter, but commented that on face value, serving on both panels does not appear to be a conflict.

Dr. Oleske noted that if CFSAC members are asked to serve on the CDC review panel, they could always opt to resign from CFSAC if serving on both would be a conflict of interest. He

said that CFSAC should choose the names of people who know what they are doing, can do the work, and have a track record. He and other CFSAC members agreed that each person on the committee would submit to Dr. Parekh the names of five people to serve on the CDC review panel. They also agreed that CFSAC members could nominate themselves.

Ms. Artman steered the discussion to areas for the peer review. She suggested that the CDC panel review the mechanisms of investigation at the agency that may be overlapping research that has already been documented. She gave the example of cognitive behavioral therapy—a field in which much research has been done to support the therapy's use for CFS. She suggested that the CDC review panel examine whether such well-researched fields are being funded at the expense of areas with gaps in the research. **Dr. Jason** urged caution when citing research fields, noting that while clinical behavioral therapy has been well-researched, there is also the impact of behavioral therapy on the immune response and endocrines. Ms. Artman clarified her statement, noting that the CDC peer review panel should examine the topics being investigated and find out where there are gaps in research. **Dr. Cavaille-Coll** asked Ms. Artman to clarify that she was suggesting an evaluation of the gaps in CDC programs, not in extramural research. She confirmed that she was discussing specifically CDC and nothing outside of CDC.

Dr. Snell said that it might be useful for **Dr. Reeves** to share with CFSAC some of the areas in which CDC needs help or is not doing as well as it would like.

Dr. Reeves: This committee knows what we're doing:

- We have a program with the objective of reducing population morbidity due to CFS. We're approaching that through surveillance studies to try to get an idea of the burden and how we can intervene.
- We're doing economics. There is an end point that can be improved and it can be used to evaluate whether interventions are cost effective.
- We have a component of the program that searches for biomarkers and the path of physiology.

The objective of the peer review is not to say that CDC should be doing this or that. We can't just all of a sudden start over again. This has been happening since 1988. This is what we believe is a logical progression. During a peer review, we will present the objectives of the program, how the program is addressing those objectives, and the committee—with background knowledge—might say, "This is not an area worthwhile pursuing." They may say, "You really need to modify your pathogen discovery efforts to do this." They evaluate what we have done and they evaluate measurable outcomes toward achieving the objective. In all reviews with which I've been involved as a reviewer and reviewee, everything that the panel says is helpful.

Part of the problem, as Dr. Miller pointed out, is does one wish to review the entire program, including health marketing, provider education, pathophysiology, in-patient studies, and surveillance? Does one wish to look at part of this program and evaluate, for example,

whether the laboratory effort is really worth it? That's one of the things that we're struggling with and that would be one type of recommendation from this committee that would help.

CFSAC should include its reasoning when it nominates candidates to serve on the review panel. Should it be looking at the entire program? Should it be looking at parts of the program? And with that in mind, who should be on the panel and what areas of expertise would they have?

Dr. Jason: I'm in full agreement with what Bill has said. The only way of choosing competent reviewers is to know what the domain of inquiry is. As I heard Dr. Miller talking about it, they're still thinking about what types of things they want to examine. At what point can we influence their process of thinking about what areas of the program they want to examine? As CDC discusses the possibilities, is there some mechanism for them to communicate that to us so that we might be able to comment on their priorities? One way that we could do that is to get a better sense of what happened during the prior evaluation. In 2007, an evaluation did occur. I'm not sure if Bill knows which areas were evaluated then. Are the same areas going to be evaluated again? Might CDC want to look at new areas for which it does not already have recommendations? Certainly having some contextual information could help us in terms of our prioritization process.

Dr. Reeves: I think that Dr. Miller said that he would try to get that particular report to this committee. That was not a peer review. That was a blue ribbon panel put together to evaluate where the program should go. It's usually an eight or nine month process to put everything together. The blue ribbon panel looked globally.

The previous peer review—I think it was probably in the late 90s—looked in quite a bit of detail at what we were doing in the laboratory. We really weren't quite where we are now. One of our quandaries is, do we want to look at great detail or do we wish to look more globally? I don't think there's an easy answer to that. We're still wrestling with exactly how that would best be done. The recommendations from this committee would help a lot. How the review is conducted affects who would best serve on the panel

Dr. Oleske: What in your mind needs further evaluation? I wish I had the expertise to tell you where the testing should be done. I would love to hear a discussion of the analyses for etiology. What has been studied enough so that people are satisfied that it is not going to give us a real handle on diagnosing this disease? What are areas that need more study? How we advise you is not an easy question and so I ask you, what are you satisfied with? What avenues of laboratory diagnostic work allow you to say, "We've looked enough into that. It's not going to give us the answer."

Dr. Reeves: I think that there probably isn't anything that we could say that about. I think the illness clearly involves a stress response, it clearly involves the HPA [Hypothalamic Pituitary Adrenal] axis, and it involves brain control of that. But we haven't completely answered those questions yet. Some of the mathematical modeling indicates that there might be bi-stability to HPA axis control of cortisol and that people with CFS max out on their stress response in that part of it and drop to a whole lower response which might have to be reset. I don't have an

answer to that. We will be seeing that in some of our studies. There are indications that the autonomic nervous system is dysfunctional in at least some people with CFS.

The genetic polymorphisms all involve HPA axis response. How are they tied in? I don't think that's answered yet. The questions on post infectious fatigue and how that kicks this over and how it might be involved—they really haven't been answered yet.

Dr. Oleske: Although I am on sabbatical, I still occasionally see adolescents with CFS. Invariably they'll come to me with lots of blood tests done at non-reputable laboratories with indications of abnormalities that just are not there. We need a list of relevant diagnostics. There are a lot of people profiteering from our patients' frustrations. There's so much being spent foolishly and wastefully on this disease. No one's giving direction as to what the appropriate agenda is for finding a diagnostic test that legitimately focuses on patients with CFS. Until we have that, we're allowing these laboratories to hoodwink and make money without accomplishing anything.

Dr. Hartz: I wonder if that's even the first step—to find a diagnostic test. I'm not convinced we know what CFS is and that we've been able to identify all of the subgroups. The subgroups may very well have different diagnostic tests or approaches and there needs to be more work on that.

Dr. Oleske: I agree with you. If we say that fatigue is the major problem, how many patients who have chronic fatigue actually had stress testing that would demonstrate at least initially that there is some post-exertional fatigue? My concern is that we don't have any standard recommendations on a workup for this disease yet. It seems to me that if we had these centers, you'd have the smart people getting together and saying, "Let's look at this."

Dr. Hanna: The ORWH is working with the National Institute on Aging to offer a grant studying fatigue. The driving point behind it is, what is fatigue and how do you measure it? Is it a deficit? I think that's a perfect vehicle for you to use.

Dr. Jason: I just want to agree with Eleanor. It's clear that some of the biological issues going on with the elderly are being mirrored in patients with ME/CFS. The program announcement from the National Institute on Aging is going to be an important initiative. I agree very much with what Arthur said about this subgrouping issue. Clearly we see patients with sore throats who get every illness that comes around, then some patients who never contract anything. These are very different types of individuals, and we need to understand their pathophysiology. Basic diagnostics is absolutely critical.

As I think about the CDC panel and how we can interact with that process, we don't really know what areas it is going to cover. We might have some kind of influence on prioritizing some of those areas. Bill has certainly mentioned some of the things that could be of interest to him and his group. I still keep wondering about the issue of the lack of individuals with medical training who are both treating and diagnosing individuals with this illness. That leads me back to the provider education program.

The CDC has had an investment in the provider education program for a long time. There's now been a new vision of the provider education program that's being launched (CME credits on the website). I think that it's encouraging to see more individuals getting onto that page. One thing that would help me try to think about prioritizing would be a better sense of the directions being taken by Bill and his group to get practitioners skilled in CFS, particularly now that they aren't connected with the CFIDS association.

Dr. Reeves: It's a hard question to answer, but it gets to one of the points that I tried to make a couple of times. We would never have started provider education had CFIDS not brought that idea forward. It was actually brought forward at this committee's predecessor. There was lots of discussion. We've gone through a lot, we've learned a lot, and even during the Education Subcommittee meeting today, you made points that we had not thought of and that we're going to have to think about. What I presented to you on education is where we are and what we know.

Dr. Parekh refocused the remaining discussion time by reminding the group of CDC's request that CFSAC provide some input on how the external review panel should approach the programs related to CFS. CFSAC could recommend including both the marketing and science aspects, said Dr. Parekh, urging the committee to take a few minutes to brainstorm about how the review process should work and the important questions that should be asked. **Dr. Snell** pointed out that if the review begins in the fall, the current CFSAC meeting would be the last time for the entire group to provide pre-review input. Dr. Parekh noted that subcommittees could be informed between meetings how the peer review is progressing.

Dr. Jason: There are so many different areas that could benefit from useful investigation. That's something that our Research Subcommittee might need to go back and think about and prioritize. In addition to getting the right reviewers, it's also about what should be the ultimate result—and that is helping people with this illness. If that's the real function of what we're all about, wouldn't it be useful if we think about bringing the leading individuals who represent organizations who have this illness into that process? If the CDC is going to be producing information that's useful, it's the patient groups that ultimately need to be involved.

Dr. Hartz: If I were involved in making recommendations to the CDC, the first thing that I would need to know is what their business plan is now—what their strategies and goals are. If I had to review every article that they've done, I wouldn't be able to digest it. I think as a starting point for developing a review committee, it would be helpful if they could have some mission statement bullet points about what CDC goals are and how it's trying to accomplish them. Then that could be critiqued. To start from scratch would be impossible, and to dive into the details of everything they've done would be impractical.

Dr. Cavaille-Coll: Bill has given us at numerous meetings a description of the program at the CDC and he's explained how it's become very broad and what the different areas are. I think that the CDC would like to have some advice from CFSAC as to particular areas of the program that should be focused on in this review. That's what I thought I heard. Am I mistaken?

Dr. Parekh: I think the CDC is asking for advice on who should be involved, the process of the evaluation, and what should be evaluated. I might have left the impression that CDC is looking to evaluate all of its programs in both marketing and science, but I think that's still unclear, so perhaps that's something that CFSAC might want to weigh in on.

Dr. Cavaille-Coll: If CDC does not have the resources to evaluate the whole system, which aspects do we think are most important? Evaluating just the laboratory program in the 1990s was a substantial undertaking, and that program is probably much larger today.

Dr. Parekh: I think that that's a fair point. There's provider education, there's the public awareness campaign, there's the surveillance projects, and there's the registries. If a choice is going to be made about what to focus on, then certainly it would be helpful if CFSAC recommended priorities.

Dr. Glaser: To me, the three most important things that need to be done to move this field forward is etiology, diagnostic marker, and new meds to treat clinical symptoms to buy us the time to do the etiology and the markers. To me this is the bottom line. We haven't gotten very far and that's where the CDC ought to concentrate.

Dr. Oleske: I certainly think we do well at measuring quantitatively. We can measure the amount of zinc in a very small fraction of blood. But what we don't do very well is evaluate how a person functions—how things work and do not work in case of CFS.

Dr. Willis-Fillinger: I've heard from a number of you that there's a lot of interest in helping providers know what works, but the bottom line is do we know what works? Is this an opportunity to look at those three things—etiology, markers, and then what actually works? Could the review assess what the priority areas are that the CDC could be working on with the resources that they have? And are there best practices ready to harvest?

Dr. Reeves: I had not thought of it that way so I cannot give you an answer. But I would like to hear what the people actually putting on the review would like to hear from the committee. What Dr. Glaser said, I agree 200 percent with. If we do not have biomarkers, if we don't know the pathophysiology, if we don't have good research in that area, we still are diagnosing based on symptoms. If we can't help the people, if we can't get some of this knowledge out there to providers, then we're not helping directly the people who are sick. Those things are not disconnected, but they are completely different areas.

We could also evaluate the overall program—what are we trying to accomplish and are we getting there the right way? That's a more overarching issue. All of these issues are worthwhile. Discussing it amongst ourselves at CDC and hearing input will help us decide which way we want to go.

Dr. Glaser: For those of us who have been in the business of hunting for a marker and getting the static that we all get back from our studies, it's a quagmire. Occasionally we get something that's statistically significant, it goes in some direction, and we publish that. But if it wasn't a quagmire, then we'd be getting some answers after 20 years. What this is telling

me is that our human definition of CFS is just that—we make it up. When it comes to stress and immunities we ain't so smart. We have to remind ourselves that there are things about the biology of the human body that we haven't even discovered yet that could be key to CFS. We just don't know, so we're shooting in the dark.

We're lumping patients together who are generating a database that's totally providing noise. So our case definition, which is a manmade case definition based on fatigue, is the best we can do. But it's not giving us a population to study that reduces the noise and the variants to the point that we can see what is going on. When I collaborate, I have to rely on my colleagues to give me serum samples that they think—from their perspective as clinicians—are the serum samples that I need to be hunting with. I'm putting my chips on the best clinicians that I can think of to give me the best quality product I can study to minimize that variance. When people take their serum samples from their patients, they treat their serum samples differently. We need to standardize those procedures as best we can to minimize the variance.

But I don't have any magical answers as to how we should define what a CFS patient is so that we get a pool of individuals who have at least something to do with each other. One way that I have done this is to focus on the acute onset patients. But I acknowledge that that's still a pretty heterogeneous population. What we need to do is focus on gathering together the best population we can get and focus on the basics—etiology, markers, and the meds that will keep our patients comfortable while we try to figure out what's going on.

Dr Hartz: I want to get back to the review process. I have not served on CFSAC long, but from what I've seen the CDC has presented very specific studies and results. What I've not seen is a business plan—these are our goals, this is how we're going to get there. If that was put together, it would be a lot easier to see what's missing, and what's not being emphasized. I think it's going to be very hard for anybody in this group to say something that the CDC hasn't heard before. They've been in this business awhile. They are well-connected with all the researchers in the field. They're going to know what the basic issues are. I think the kind of input we could give is to recommend that the review panel look at where the agency is going, how it's getting there, and maybe suggesting some changes in emphasis. I think that is an important first step if it has not already been done.

Dr. Snell: Just to go back to Bill's comments—what I'm hearing is that the CDC will do an internal overall program review to identify the areas that may then be later peer-reviewed. Is that correct?

Dr. Reeves: That's correct.

Dr. Snell: So, if you find an area in which you're not achieving what you think you should be, an outside entity may provide some insights that will help change your direction or provide ways in which you may look at things differently.

Dr. Reeves: That's correct, but the review could also go the way that Dr. Hartz has suggested. We do have a strategic plan and we do have a logic model with measurable

outputs towards controlling CFS. We also have components in the program that deal specifically with brain function, etc. It might really be more worthwhile to go through the overall program, analyzing the strategic plan and which tactics are being used without going into each tactic in detail. What we want is what will help the program deal with CFS better—get some kind of insights we do not already have. I think it would probably better on an overarching scale, but I'm not completely convinced.

Dr. Snell: One of the problems is subgrouping, but it seems to me that you've got such a lot of data that if you went back and looked at it in a different way, it might be possible to use that subgroup. If you've done a lot of brain function data and it's noisy, why is it noisy? You've got a lot of data that maybe doesn't show anything when you look at it as you have been. But looking at it another way it may indicate that yes, there are five subgroups of CFS.

Dr. Oleske: Bill, that program you mentioned before, were you talking about functional magnetic resonance testing and things like that?

Dr. Reeves: Yes, I think that I presented that here during the previous meeting. The in-patient study that we're doing at Emory will have two days of fMRI, one of those days during a cognitive function to look at brain regions that light up; the other during a cognitive stressor to look at pathways. Then that's going to be linked to the social stress test, which is going to be looking at HPA axis function and autonomic nervous system function and cytokines every 15 minutes.

Dr. Oleske: And these are going to be patients that you've characterized as having CFS?

Dr. Reeves: We're going to be looking at 30 people as clean as we can get, but with CFS diagnosed by the research case definition. We will have 60 controls.

Dr. Reeves noted that the committee discussion had been enlightening for all participants and hoped that CFSAC members could use discussion time the following day to come up with recommendations for the CDC external peer review.

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

Health Resources and Services Administration Update

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

HRSA is considered the healthcare access agency. HRSA funds infrastructure and healthcare services for people who are uninsured, underinsured, and others in this country in need of healthcare services. HRSA focuses on women and children, people living with AIDS, urban and rural populations, critical access hospitals—the healthcare safety net.

As far as our programs in general, the minutes on page 24 of our November 2007 meeting basically says it all. There's really not much new. HRSA is continuing its commitment to ensuring that programs that are funded provide high quality healthcare and are in keeping with the evidence base. HRSA also is continuing to focus on quality improvement and performance measurement across the agency.

HRSA is launching a new learning collaborative on patient safety that is designed to test best practices involved in patient safety and medication management across the country. We're recruiting two or three teams per state. HRSA is looking for teams that have some impact on medication management. In other words, someone involved in providing medications to patients. For example, in our local geographic area, HRSA is looking at tracking a patient. Where do they go when they get medication? They may go to the pharmacy or Walmart to treat a cold on the weekend. They may go to a specialist, a hospital emergency room, or their primary care providers. The idea is to gather together the team of individuals who are involved in that patient's care and get them to think about the handoffs in medication reconciliation, etc. HRSA will be enrolling teams over the next month or so, so if you're interested in participating, let me know.

Dr. Willis-Fillinger noted that CFSAC expressed interest in the role played by HRSA's Bureau of Health Professions in provider education. She introduced **Dr. Daniel Mareck** to discuss his agency's focus.

Dr. Daniel Merrick, Chief Medical Officer, *Bureau of Health Professions, HRSA*
Accompanying Document: *Bureau of Health Professions Collaborative Opportunities*

I'm a family medicine physician by training who is originally from Minnesota. I've been working in HRSA for two-and-one-half years, first for the National Service Corps and now for BHPr.

HRSA is involved with health professionals on the supply side of the equation. There's a federal interest in the healthcare workforce because there's a persistent need in underserved, underinsured, minority, and disadvantaged populations throughout the country in both urban and rural settings. HRSA grew out of a Federal push in 1970s for safety net programs including the community health center programs, the National Service Corps, and in BHPr, the Area Health Education Centers. AHECS are focused on service, education, and training issues for primary care clinicians.

Factors Affecting Health Workforce Shortages and the Need for BHPr

- 36 percent of active physicians are age 55 or older.
- As the workforce ages, the population ages, and technology advances, there is an increasing demand for medical services.
- 20 percent of the U.S. population lives in rural areas, but only 9 percent of physicians practice there.

HRSA focuses on getting the workforce into the appropriate settings, then retaining them in the areas where there is need. BHPr would like to increase the diversity of providers and the competency of the provider workforce. That's where I think the potential for interaction between BHPr and CFSAC comes into play. Our objective is to get the right people with the right skills in the right places to achieve the right health outcomes.

BHPr-CFSAC Collaboration

HRSA is not focused on clinical practice. The agency funds grant programs with 1,200 institutional grantees. The first three programs listed below appear to be the most relevant to CFSAC, but the committee can decide which would be most appropriate for disseminating provider education information. This list is based on FY 2007 data:

- Advanced Education Nursing Program – 134 grantees and almost 6,000 nursing students enrolled.
- Primary Care Medical Education – More than 300 grantees, which is the largest number of total grants in BHPr. The ultimate goal of these grants is to improve access to care.
- Title VII, Section 747 – Includes six separate programs. Those most conducive to collaboration with CFSAC are:
    - Predoctoral Training in Primary Care – purpose is to plan, develop, and participate in predoctoral programs in family medicine, general internal medicine, and/or general pediatrics.
    - Residency Training in Primary Care – purpose is to plan, develop, and participate in approved residency programs.
    - Physician Faculty Development – training of physicians who plan to teach in primary care via Clinician Fellowships, Master Educator Fellowships, and Community Preceptor Faculty Development. Includes clinician research fellowships.
- Academic Administrative Units – relate to the development of clinical academic infrastructure in primary care areas such as family medicine, general internal medicine, and general pediatrics.
- Physician Assistant Training
- Residency Training in General Pediatric Dentistry

AHECs – the best vehicle for CFSAC dissemination of provider information.

Four main activities:

- Student recruitment at the K-12 level as well as in baccalaureate and community college settings to get individuals into the health workforce in all areas, not just medicine and dentistry. Other areas include physician assistant, nurse practitioners, nurse midwives, social workers, and behavioralists.
- Health professions students' clinical rotations, which are community and academic partnerships that help facilitate community placements for health profession students coming from academic areas to work in underserved community settings, both urban

and rural. AHEC assists with preceptor recruitment for these students and finding places for them to stay during their rotations in the hopes that they will have positive experiences training in the underserved locations and will want to go back there to practice.
- Residency clinical education and training relating most specifically to physicians in post-MD residency programs.
- Continuing educations activities. These are usually developed locally in community settings. These are community-academic partnerships, so a lot of the CE activities that go on in AHEC centers are developed locally based on clinician or provider needs in those specific areas.

Additionally:

- AHEC grants require a state or local dollar-for-dollar match.
- There are 53 AHEC programs as of October 2007 in 46 states and the District of Columbia. Some states have more than one program and the following states have none: Kansas, Michigan, North Dakota, and South Dakota.
- 42,854 health professions students have been trained in community settings and over 313,000 healthcare providers have received continuing education including webinar and self-study programs.

Geriatric Education Centers (GEC)

- Structured similarly to the AHECs in that they are academic/community partnerships. There are currently 48 GECs across the country. The funding stream for GECs has been uncertain recently (the program was defunded in FY 2006), but a lot of the states have put their own state, local, and academic resources into the program and have kept them going.
- More than 145,000 health professions students, faculty, and practitioners have been educated.

Public Health Training Centers (PHTCs)

- 14 centers across the country. Have not been particularly involved in CFS initiatives.
- PHTCs are located in 44 states and the District of Columbia.
- More than 280,000 public health workers have been trained since 2001.

Preventive Medicine Residency

- Not a crucial player in CFS, but it is another dissemination vehicle.
- Plans and develops new residency training programs.
- 41 residents were involved in 2006; 48 percent of them entered practice in underserved communities.
- There have been 1,598 preventive medicine graduates of the program since 1986.

National Research Service Awards

- 19 institutional grantees.
- Program has just been restructured from five-year awards to the new three-year awards that will be made this summer. This year a competitive grant cycle has occurred and will be funded initially by NIH's National Research Service Award (NRSA) program. One percent of NRSA money goes to AHRQ and one percent comes to HRSA. The part that comes to HRSA is designed for primary care research development. As a result, one of the institutional criteria for an NRSA award is that the institution must have a history of having received a Title VII Section 747 grant to document an interest in primary care.
- About 100 postdoctoral trainees receive support each year. The award provides stipend and tuition support for primary care researchers. Most do two years of research as part of their award.

Committee Discussion

Dr. Oleske: There are so many Americans without healthcare and so many underserved individuals. Patients with CFS are not always underserved because of finances but because there are no physicians to take care of them. Do you think that medical school programs that have people interested in CFS such as those in Miami and Nevada would be eligible to apply for a training program with a disease-specific focus like CFS?

Dr. Mareck: Our programs are pretty wide open. Grantee applicants have submitted applications regarding all sorts of high-risk populations. For the six training programs under Title VII, Section 747 programs, one of the review criteria is called Special Considerations. The following statement about this criterion is written into the program's authorization bill:

"The extent to which the proposed project responds to preparing practitioners to care for underserved populations and high-risk groups such as the elderly, individuals with HIV/AIDS, substance abusers, the homeless, and victims of domestic violence."

HRSA has an emphasis as well on:

"The extent to which the proposed project responds to preparing practitioners' specific training and/or learning experiences to develop knowledge and appreciation of all cultural and language influences, health literacy improvement, and the delivery of high-quality, effective, and predictably safe healthcare service."

There's no reason, at least as I read both the statutory language and the HRSA emphasis, that people couldn't put in specific grant requests for CFS or any other kind of illness as long as there is an emphasis on underserved populations. All of our grants are competitively reviewed, so we have outside experts in these areas. As I see it, there's certainly flexibility there for any kind of emphasis on a disease as long as the appropriate populations are underserved.

Ms. Artman: If a patient group is interested in asking HRSA to conduct a CME program for local providers so patients have access to care, is that something that would fall under your CE program?

Dr. Mareck: It would, although it would work better if the patient group contacted its local AHEC, related that patients are not sure that their providers are adequately trained, asked how to get information out to providers, and requested getting a program sponsored. It would be more effective as a local initiative.

Dr. Hartz: One of the reasons that there is a shortage of physicians that know about CFS is the economics. There are very strong economic disincentives to taking care of these patients. Is there anything that HRSA can do to provide stable funding for physicians who want to take care of these patients?

Dr. Mareck: To my knowledge, no. The funding is legislatively driven. You might check with HRSA leadership, but a lot of funding is based on what comes to us legislatively. I don't think that it's realistic to expect that HRSA would carve out X amount of money for this or that emphasis.

Dr. Hartz: In other words, you don't think it's within the scope of what HRSA was set up to do?

Dr. Mareck: Exactly. We administer the programs that are designed to help with training practitioners for the underserved. As you are aware, this Administration has been particularly interested in the Community Health Center program and has put some extra resources into development and expansion of these centers as well as the National Service Corps. Our programs are supported as well, but in times of limited resources, there's only so much you can do. We collaborate with those programs because a lot of the people who we train wind up practicing in Community Health Centers.

Dr. Marcia Brand, the Associate Administrator for Health Professions, has a particular interest in collaborating across agencies that encompass Community Health Centers. There is no reason why CFSAC cannot conduct a dialog with her.

Dr. Jason: Your presence before this committee is really key because we've been talking about medically underserved issues this morning and at prior meetings. One of the issues is that there is such a small number of medical personnel who treat individuals with ME/CFS. I would say that this problem is probably more stark for CFS patients than for just about any other illness group.

Another issue is the fact that when CFS research is done, the sample is often small. Researchers don't find markers because they are not consistent across the entire sample. When a medical reason or biological marker cannot be found, these people are stigmatized as having a psychogenic illness.

What's really needed is a network of locations from which researchers can draw hundreds of samples and observe the disease subtypes that are critically necessary. Could we get some information from your organization on how many grant applications have actually come in where CFS patients or practitioners have been identified and how many have actually been funded? Are there any opportunities for collaborating with your agency at a high level where we could start thinking about the types of critical networks that are needed?

Dr. Mareck: At my level, I wouldn't be able to comment on moving forward with a specific research focus. That would be a discussion about policy priorities that would occur above my level. In terms of numbers of grantees who have put in proposals for chronic fatigue over X period of time and how many have been funded—that sort of information would be available, because we track our grantees with performance measures. The AHECs could also be surveyed to determine how many CE programs have been done related to CFS.

Ms. Healy: I wondered if in any of the Title VII programs there is any statutory language about chronic diseases. Might advocacy groups be able to go to Congress and ask for the same sort of language in the Title VII training grants? Could language be added to grant applications that, for example, might require awardees to select from a list of diseases for their grant focus? What advice would you have for CFSAC or advocates who might want to work on the legislative side to get the language into the guidelines?

Dr. Mareck: It would not be my role as a member of the Executive Branch to comment on the legislative side of things. Although I have not reviewed all of the guidelines, I'm not aware of any statutory language in the grant programs that targets CFS or any other specific chronic disease other than HIV/AIDS.

Dr. Bateman: What would it take for HRSA to validate that people with CFS are an underserved population based on CDC numbers? How could we include language so that it somehow attracts people to submit grants?

Dr. Mareck: I don't know what it would take to specifically do that. What we could do initially at BHPr is be a disseminator of information to the mechanisms that are already in place.

Dr. Bateman: We devised a letter and proposed that the Surgeon General (SG) send it out to institutions. Would HRSA be willing to make that letter fit your agency and disseminate it? It's a letter saying that there is a critical need and directing people to the CDC website.

Dr. Mareck: In terms of HRSA disseminating such a letter, there would have to be an internal discussion through the department and HRSA leadership, but it certainly could be done.

Dr. Bateman: If there's a show from HRSA that you recognize this illness as an underserved group, that in turn might set the ball rolling for people to realize that their grants may be noticed. For students who want to train, this might be an avenue for them to get funding.

Ms. Artman: Even if you didn't send the same letter, that link to the CDC website that has the free CME program is what we're really trying to get everyone to participate in. Is there at

least a way for people who receive grants from you to get that link? Even if you're not saying it's a CFS link, it would be out there for anyone who wants free CME.

Dr. Mareck: Potentially we have more than 1,200 institutional grantees, so certainly through our various email addresses that our project officers have with these grantees, links like that certainly could be disseminated after being properly vetted with agency leadership.

Dr. Oleske: Are most of the physician training programs for underserved areas with high needs applied for through departments of medicine for fellowships or residencies or other medical school mechanisms? You obviously train nurses in different areas. Does that mean that nursing schools apply for that support for training?

Dr. Mareck: Our Division of Nursing administers most of our Title VIII grants having to do with nursing education and development of nurse practitioners and midwives. In terms of the medicine/dentistry grants, we focus most on primary care; these grants would be found in general internal medicine, general pediatrics, and med/peds. We have behavioral and geriatric grants as well. The AHECs are collaboratives and the bulk of grants go to medical or nursing schools, but then there are 221 AHEC community-level divisions, so there is an avenue of dissemination that way.

Dr. Oleske: It looks like this might be a two-way street. If we had centers, they could use this mechanism to get support for trainees. The problem I see now is that we don't have the infrastructure to apply except if we also happen to be friends with the residency director programs. Is there a way, though? These are sympathetic training programs that are committed to serving underserved populations.

If we could provide you information from the CDC numbers that shows you that this is an underserved population, we may not yet be in the position to have Centers that could actually apply for that money, but certainly our medical schools and nursing schools could, if they were informed of this, receive funding that would at least reach out to some of the patients who are underserved right now.

Dr. Mareck: That would take a bit of a paradigm shift from the standpoint that, at least historically, BHPr has had an emphasis on primary care and the underserved. Unless it comes to us in statutory language, BHPR has let the grantee applicants say how they plan to spend the funding rather than say, "We specifically want you to emphasize A, B, and C."

Mr. Newfield: I want to try and implement what Lucinda and Rebecca were saying. Anand, how to we effectuate that? He's saying that it needs to be vetted. Is that something that we need to do as a recommendation, is that something that we can put onto Deborah's lap?

Dr. Parekh: It needs to be a recommendation. I think that there needs to be some discussion about the letter, learning more about what it is you would want HRSA to do, learning more about all of the programs available, and making sure what information you want HRSA to disseminate. Then it would be a recommendation to the Secretary, and the Secretary would pass it on to the HRSA Administrator.

Dr. Jason: Could CFSAC make a recommendation to the Secretary to instruct HRSA to make CFS a priority just as the agency has with HIV with the intention of getting the types of centers that we need implemented through HRSA?

Dr. Parekh: I think recommendations are best when they are quite specific and they're an actual task or action. For example, perhaps a targeted letter based on the fact that Dr. Mareck said the programs might be open to the CFS materials being disseminated. That's something more targeted. A recommendation as broad as saying that HRSA should prioritize CFS probably wouldn't be as effective as something more targeted.

Dr. Oleske: We could come up with a way of at least alerting centers that are funded through HRSA programs like this that they could possibly include CFS.

Social Security Administration Update

Sharon Shreet, *Senior Advisor to Office of Associate Commissioner, Office of Employment Support Programs, SSA*
Accompanying Document: *Ticket to Work: New Program – New Opportunities*

The mission of the Office of Employment Support Programs is to help SSA disability beneficiaries who want to become more self-sufficient through work. There are several underlying beliefs that direct what we do:

- Beneficiaries have the right to self-directed, inclusive, and supported lives.
- Work has intrinsic value for everyone with and without disabilities.
- The mix of benefit payments and income from work provide an essential tool to beneficiaries to maximize their self-sufficiency.
- Maximizing self-sufficiency is an incremental process that has breaks and plateaus.
- Community partnerships are essential to us in achieving our mission.

Ticket to Work Program

- **The major program in the Office of Employment Support Programs.** Ticket to Work is for people who have already been determined to be eligible for either the Social Security disability benefits—Supplemental Security Income benefits or the Social Security Disability Insurance (SSDI) benefits. It's a voluntary program that provides beneficiaries with a vocational voucher ("ticket") that they can use to get the services that they need in order to return to work. They receive the services from a participating provider organization that we call an Employment Network (EN).

- **ENs can be almost any public or private organization.** The only type of organization that cannot become an EN is a Federal agency. ENs include private companies, state and local governmental agencies, centers for independent living, one-stop career centers, Goodwill affiliates, hospitals, and universities.

- **Ticket to Work differs from previous programs** that reimbursed the provider for the costs of providing services. Under Ticket, the payments to the provider are set amounts paid by SSA as the beneficiary reaches certain employment goals. Payment amounts do not depend on what services ENs provide or the cost of those services.

- **Ticket to Work was started by legislation signed into law in 1999** and has been recently revamped. It has been a challenge for us to get enough ENs and keep them operating so that people have a true choice as to where to receive services. We believe this was caused by the original payment structure, including the amount of payments that could be received by the organizations and the amount of work that was required by the beneficiary before the EN could qualify for payments.

SSA proposed new Ticket regulations that are currently under OMB review. We expect to get them published sometime this spring:

- Eligibility for Ticket to Work will extend to all those eligible for SSDI and to all supplemental security income beneficiaries with disabilities who are between the ages of 18 and 65. Right now, people who are categorized under "medical improvement expected" do not become eligible for a ticket until they've had their first re-determination or continuing disability review.

- Eligible beneficiaries automatically receive a ticket. Those who are interested in using it contact a participating EN to see if they can come to an agreement on what services would be needed and provided in order for the beneficiary to reach his/her work goal.

- It's totally voluntary on the part of the beneficiary and the EN. The beneficiary chooses whether or not to use the ticket and if he/she chooses to use it, the person also chooses what organization to work with in order to get the services needed to go back to work. A successful relationship is one in which there is a good fit between services that the employer can provide and those that the beneficiary needs to meet his/her work goal.

- Services often include rehabilitation and transportation, adaptive devices, job placement and follow-up, and training. The ticket holder and EN work out the details. SSA doesn't prescribe that certain services be included and we don't limit the services that can be included.

- The EN is not allowed to charge for any of the services that are in the agreement. SSA makes payments to the EN as the beneficiary achieves certain milestones or outcomes towards work.

- While the beneficiary is using his/her ticket, SSA will not initiate a continuing disability review for medical reasons.

- Other SSA work incentives continue to apply while the beneficiary is using the ticket. These include impairment-related work expenses, plans for achieving self-support, and student earned-income exclusions.

- Payments are made to the EN in three phases as the beneficiary reaches certain goals:

    - In the Phase 1/Milestone 1, the employee only needs to earn $335 for work in two weeks in order for the EN to get a payment of $1,177. In order for that EN payment to continue, the beneficiary must meet milestones of earning $670/month for three, six, and nine months.
    - Phase 2 is when the beneficiary is earning at the level of substantial gainful activity (SGA), which is $940/month. During Phase 1 and 2, the beneficiary may still be receiving benefits.
    - Phase 3 kicks in once the beneficiary has worked through his/her trial work period, is found to be able to engage in SGA, and is no longer receiving benefits. If the EN and beneficiary work together until the person has totally worked him or herself off of SSA benefits, there's a potential for the EN to get $20,000-$21,000 in total benefits.

- Community cooperation will be easier under Partnership Plus. Currently under the ticket program, there is friction between state vocational rehabilitation agencies and community organizations that might want to be ENs, because they're competing for the same beneficiaries and the same funds. Under the proposed regulations, the individual will be able to get services from a state vocational rehabilitation agency without assigning his/her ticket to that organization. The agency can be paid under the cost-reimbursement method and the person can save the ticket to use with a community organization or other EN.

The program's goal is for beneficiaries to be successful in work, not earn a certain amount of money so that services can be cut off. We want beneficiaries to continue to be able to get the supports that they need.

We had a Ticket Partnership Summit in March in Louisville, KY, to bring together community partners and a variety of organizations. About 450 people attended who are now going into the states and serving as ambassadors to talk about the ticket program and spread the word about the new regulations.

We also provide grants to 104 community organizations. The funding is for Work Incentives, Planning and Assistance Projects to provide information about how benefits will be affected and what work incentives will be provided to help individuals get back to work.

Beneficiaries can also get information about the ticket program and other work incentives and get help with employment related legal issues from 57 protection and advocacy organizations that we fund—one in every state and territory.

The Web address for program information: www.socialsecurity.gov/work

Committee Discussion

Dr. Oleske: This sounds like a wonderful opportunity for people who have been disabled to go back to work and test the waters. If they're able to generate some of their income, it sounds like they then give up some of their benefits. What happens if someone tries it and never gets past Phase 1, or a person feels that it has been a mistake, can't tolerate it, and wants to move back onto full benefits? I'm looking for the punitive side, because I'm always expecting to see a punitive side.

Ms. Shreet: The beneficiary can participate in the program for as long as he/she wants and if the person decides to drop out at Phase 1, then the EN gets no further payments other than Phase 1. As far as how it affects a person's benefits and their ability to continue—that's a really scary thing for a lot of people, because the rules are very complex. And that's why we have the work incentives planning and assistance (WIPA) organizations, so that they can work with an individual and say, "In your particular situation…" Because it depends on how much the person may have worked in the past, whether he/she has used up any of the trial work period in the past, whether the person used other work incentives, and what kinds of benefits he/she is receiving. The WIPA organizations will say, "In your particular situation, this is exactly what will happen under various scenarios."

Dr. Bateman: Can someone stay indefinitely in Phase 1?

Ms. Shreet: Someone can stay in Phase 1, but the payments to the EN won't go higher. If the person continues working at $640/month, he/she won't have worked to SGA.

Dr. Bateman: So it's not time sensitive?

Ms. Shreet: It's not. For some people $670/month might be right, and we encourage them to do what's right for them.

Ms. Artman: With this illness, people tend to push and crash, so someone could work for four hours today and be out for three weeks. It's not really an employer friendly illness. No matter what accommodations are made, few people want to hire someone for four hours. I've noticed on the SSA website that if someone decided to be self-employed that they can't work more than five hours a week. Do you know anything about that, and can you explain that big difference between 5 hours of self-employment and $700/month?

Ms. Shreet: I'm not an expert on that, but I'll have someone contact you.

Fran Huber and Mark Kuhn, Policy Analysts, *Office of Compassionate Allowances and Listings Improvement, Office of Disability Programs, SSA*

Accompanying Document: *Chronic Fatigue Syndrome: It's more than being tired all the time*

We are part of a work group that has been convened in our office about CFS. We are going to show you how we educate our adjudicators about CFS in order for them to process claims. They must wade through a lot of medical evidence to try to figure out whether or not someone who's making a disability application alleging CFS or alleging other conditions along with CFS is eligible for benefits. This training is also available in the video on demand training portion of our internal website for our adjudicators. These are the people who are processing the initial applications for disability benefits. The training is also for people who are hearing the appeals if initial benefits are denied.

Education Objectives

1. Medical Overview of CFS

- SSA recognizes CFS as a medically determinable impairment.

- We want to make sure that people understand the different things they may see in the medical record. At the initial determination phase, the examiners contact all of the medical sources that the claimant provides to us and often gets a lot of medical evidence in return. W are training them to look for not only things called CFS but also chronic fatigue immune dysfunction syndrome (CFIDS) and myalgic encephalitis (ME)

- This is a diagnosis of exclusion, which means that examiners should expect a lot of medical evidence. They may get a lot of records back from medical sources that state what the person does *not* have. In the case of CFS, this supports the diagnosis.

SSA relies on the CDC's definition of CFS. We tell our adjudicators to look for the presence of clinically evaluated, persistent, or relapsing chronic fatigue. In addition:

- It must be of new or definite onset.
- It cannot be explained by another physical or mental disorder.
- It is not substantially alleviated by rest.
- There is a reduction in previous levels of activity (occupational, educational, social, and personal).
- There is a concurrence of four or more of the following:
    - Self-reported impairment in short-term memory or concentration.
    - Sore throat or laryngitis.
    - Tender cervical or axillary lymph nodes.
    - Muscle pain; multi-joint pain without joint swelling or redness.
    - Headaches of a new type, pattern, or severity.
    - Unrefreshing sleep.

- Post-exertional malaise lasting more than 24 hours.

A presentation from the CDC is incorporated into the SSA video on demand presentation showing what kind of process someone with CFS may go through when being evaluated by a physician for CFS. This includes an explanation of the extensive medical workup, a mental status exam to evaluate changes in cognition, and laboratory findings such as blood and urine workups.

If there is a suggestion in the medical evidence of another explanation for fatigue, our examiners follow up on that.

Although there may not be a diagnosis of CFS, there may be a diagnosis of idiopathic chronic fatigue, which basically allows for the fact that the person is fatigued but medical personnel do not know what the fatigue is attributed to.

SSA uses Social Security Ruling (SSR) 99-2p to make clear to our examiners what it is we are looking for. Our definition of disability is statutorily driven: disability is the inability to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment or combination of impairments which can be expected to result in death or has lasted or can be expected to last for a continuous period of not less than 12 months. In addition the medically determinable impairment must be established by medical evidence that consists of signs, symptoms, and laboratory findings and not only by an individual's statement of symptoms.

Here are some examples of the medical signs that we instruct our examiners to search for in the medical evidence that will support the determination of a medically determinable impairment:

- Palpably swollen or tender lymph nodes.
- A red throat or complaint of throat soreness.
- Persistent, reproducible muscle tenderness on repeated activity.
- Any other signs that are consistent with medically acceptable clinical practice.

Here are some examples of lab findings for CFS that examiners may find in the medical record:

- An elevated antibody titer to Epstein-Barr virus, capsid antigen equal to or greater than 1:5120, or early antigen equal to or greater than 1:640.
- An abnormal magnetic resonance imaging brain scan.
- Neurally-mediated hypotension as shown by tilt table or other clinically accepted test
- Any other laboratory findings that are consistent with medically accepted clinical practice and are consistent with the other evidence in the case record.

We ask our adjudicators to look for medically documented signs and symptoms that may indicate some of the ongoing mental or cognitive problems that are reported such as changes or difficulty with:

- Short-term memory and information processing
- Visual-spatial perception
- Comprehension
- Concentration
- Speech
- Word finding
- Calculation
- Other symptoms suggesting persistent neurocognitive impairment

In our system, having a diagnosis in the medical evidence that says the person has CFS is not sufficient to establish eligibility for disability. The medical history, medical signs, and laboratory results must be consistent with the diagnosis.

First there must be a medically determinable impairment established. The preceding laboratory findings or medical signs would support this determination.

Once a medically determinable impairment has been established, the second part is determining the severity of the illness and the impact on the person's function. We ask our examiners to look for things like:

- Non-pharmacologic therapies (exercise, aquatic therapy, stretching). Lots of times when people are receiving these kinds of therapies, there are reports from those healthcare providers that help to support the claimant's allegations of disabling fatigue and other symptoms.

- Medications in the record that indicate that the person is being treated for something that supports the diagnosis. We also ask our examiners to be certain that the medications are prescribed for an underlying pathology. All medications can cause side effects that lead to other symptoms.

- Distinguishing between fibromyalgia and CFS. CFS is a diagnosis of exclusion and FMS is not. In general, if the major presenting complaint that brings the claimant to medical care in the first place is pain, then the condition is likely FMS. If the major complaint is fatigue, the condition is more likely CFS.

We direct our examiners to the AHRQ website for the *Systematic Review of the Current Literature Related to Disability and Chronic Fatigue Syndrome* published December 2002.

2. How does SSA Evaluate Evidence from a CFS Claim?

SSR 99-2p also guides this evaluation. The types of evidence that examiners should be examining in CFS cases include specific medical evidence regarding functional capacity:

- Physician observations during exams.
- Evidence of the claimant's functioning, including their own self-report.

- Treatment history.
- Persistence and consistency of subjective complaints.

These are the kinds of documents that we look at to make sure that the person is eligible after it has been established that the claimant has a diagnosis that is a medically determinable impairment. These show how CFS is affecting the person's function.

Committee Discussion

Mr. Newfield: Has there been other regulations since SSR 99-2p supplementing that?

Ms. Huber: No. One of our work group functions is to find out whether or not that needs to be updated.

Mr. Newfield: Is it part of the work group to say whether you might define further laboratory tests in the "other" category so that it might be specifically delineated versus just in the ambiguous spot that it is?

Ms. Huber: Absolutely. We're trying to find any kind of diagnostic criteria that would be helpful for us to be able to put somebody in a medically determinable impairment group.

Mr. Newfield requested data on how many adjudicators have accessed the on-demand training video, and Ms. Huber replied that she would look into getting him the number. She added that the video was created in October 2005. Ms. Huber also noted that the working group hopes to reach a conclusion on updating SSR 99-2p by the end of the summer. Mr. Kuhn added that the work group has finished surveying the regional offices and DDS to ask them how effective the training video is and whether they are using 99-2p successfully. Respondents have made some suggestions and the working group will be taking those into account as it updates training.

Dr. Jason requested data from the last few years on how many people with CFS have entered the Ticket to Work and disability programs, been denied, appealed their denial, and attempted to reverse the denial by appealing it under another illness because they thought that it would be easier to get disability.

Ms. Huber said that such information is not easy to obtain because SSA does not have a medical listing, which makes the database hard to search. The problem is compounded because when adjudicators make their decision, they enter it on a form called an 831. On that form, they are asked to put a primary and a secondary diagnosis. If they use CFS, then SSA can find it. If there are some other co-morbidities and adjudicators use those diagnoses instead, then SSA won't be able to find CFS listed. The only other way search for the information is to open every case and do a word search, which is impractical. Ms. Huber concluded that she would make a suggestion that the coding be more specific.

Dr. Jason asked whether it was possible for the work group to track what the claimants say they have, follow what happens to those individuals, and then present CFSAC with the data

following CFS claimants over time. Ms. Huber replied that such information is in the application, but the application is not necessarily searchable yet.

Mr. Newfield asked whether claimants can request to see their 831. Mr. Kuhn said that 831s are part of a claimant's case file and are available to the person. If a claim is denied, the person receives a letter stating the reasons for the denial and what course of action to take.

Dr. Oleske: As a physician who has had to appeal several denials, I'll have to say that it sounds like there has been a marked change in how SSA is addressing CFS. Just a few years ago, it was more of a fight to get benefits than it now sounds. It sounds like you're very sympathetic to the diagnosis and the difficulties we have as clinicians. Since I'm on sabbatical now and not actively taking care of the patients, I don't know if it's improved as much as it sounds like it's improved, but I'm very impressed because it used to be a long, drawn out affair to fight for our patients to get disability. Now it sounds like SSA has decided to accept the arguments that we make when we support a patient who has CFS.

Mr. Newfield: Now you just fight an insurance company and not both, right?

Dr. Bateman: It's improved a great deal for patients seeking disability once they have reached the administrative hearing stage. I can understand that if they have a new onset of illness that the delay is helpful to understand that people are truly disabled, but a lot of our patients are in a stable state of chronic disability at the time they start to apply. What kind of evidence would it take to allow patients to be awarded their disability the first time they apply? I tell my patients that it's a one to two year process, and their finances are decimated.

Ms. Huber: The biggest hurdle for our examiners is processing the information on making the diagnosis quickly enough for the claimants. The more clearly the diagnostic criteria we have, the easier it is for us to get past that medically determinable impairment and then be able to examine the total evidence from the claimant and other health practitioners. The statute says that we have to have a medically determinable impairment first and that has to be determined by physicians.

Dr. Bateman: But with all due respect, I do believe that if all that is present when they first apply, they're still going to receive the first and second rejection because apparently those examiners don't have the same authority as an administrative law judge (ALJ) to make a decision in the case. Even if all that is present, it's a guarantee that patients are going to go to that ALJ phase or the third phase before they are awarded—at least where I am.

Mr. Kuhn: One thing that certainly would help is that if there are biomarkers or if there are some cytogenic tests—if there's just something that we can use that produces another medical sign. Also, even if you were to discover biomarkers, they have to be in the medical evidence for our adjudicators.

Dr. Bateman: I recently gave a CLE talk to disability lawyers and ALJs. Basically what I did was took the 99 2-p and then I expanded the areas of what I thought could be added as objective markers and tests. I think that even though we still have non-specific markers, if

you could include more examples for the judges—we still have lots of findings that could be in the chart. Educating that community on the progress in the last five years would be very helpful.

Ms. Huber: That's what our work group is all about, so please do send that information on.

Dr. Snell: Do you keep data on reasons for denial? A compilation of that data would be interesting for us to look at. Is it primarily considered a misdiagnosis or does the level of functionality come into it?

Ms. Huber: That information is on the 831, but I don't know if it gets down to the level of specificity that you might be thinking.

Mr. Kuhn: In general terms, it could actually be that at that point, it's been determined that they can do sedentary work. There may have been a determination between the adjudicator and the medical consultant that in fact the person does have CFS; however, after looking at the rest of the evidence in the file regarding that person's residual functional capacity, they may determine that the claimant can do sedentary work and in order to be determined disabled, a person would have to be determined to be able to do less that sedentary work.

Ms. Huber: In the disability system, it's all or none.

Public Comment

Joseph, New York

I am 33 years old. I may look healthy, but I have had CFS for 4 years, 3 months, and 4 days. On the day I got it, Feb. 1, 2004, my life changed forever. Prior to getting CFS, I was a healthy 29 year old college professor who had a great social life and many hobbies and interests. In the time since getting CFS, I have felt sick every day. I've had to give up much of my life as I knew it. CFS is such an inadequate name for this illness. I told a friend that I have CFS and she said, "Oh, I have that too. It's called being married with two kids." Those of us who suffer from CFS are physically sick. Fatigue is one of, although not the only, symptom of our illness. Other symptoms are different for different people. My symptoms have included fatigue, muscle ache, back ache, headaches, chest pains, digestive problems, heart palpitations, and heart arrhythmia. Prior to getting CFS, I had none of these symptoms.

Since having CFS, I have seen many doctors from many different fields, and I've tried numerous treatments, spending tens of thousands of dollars along the way. None of these doctors or any of these treatments has made me feel even the slightest bit better. I have come to see that the only thing that we know about CFS is that we don't know. This clearly needs to change. Reactions that I've gotten from doctors have ranged from telling me the problem is all in my head to telling me they'll absolutely heal me and not doing so. The medical community needs help in dealing with this illness both in terms of treatment and of bedside manner.

Since getting CFS, I have not been in control of my life, CFS has. People tell me 33 is the prime of your life, but I feel like my life is over. For the first three years I had CFS, I could only work part time. Fortunately, I lived in a family-owned home so my living expenses were low. In February 2007 my financial situation changed and I had to take on a full-time job. It was then that I understood what a friend who had CFS meant when he said to me, "People with CFS can either have a job or a life, but not both." I have all to do to force myself out of bed in the morning and push myself through each day. An afternoon nap is a must, and by the time Friday rolls around, I can hardly function. From what I hear, I have one of the less severe cases of CFS. Some can't work or even leave their home.

CFS is a very deceptive illness. We don't appear to be sick to people, so people sometimes lack empathy. One of the worst parts of having CFS is how I now feel at my worst when doing the things I used to enjoy doing the most—summer (hot weather), playing sports, nightlife, dating, and sex.

My recommendations for CFSAC would be the following:

1. Recognize and approach CFS for what it is—a physiological, not a psychological illness.
2. Encourage doctors to think outside the traditional box when treating CFS patients.
3. Research, research, research.

In November 2007 I developed atrial fibrillation, which is an irregular heartbeat. Many people who have CFS suffer from rapid or irregular heartbeat but no one yet has been able to define or explain the correlation. It amazes me that we can put a man on the moon, we've performed successful heart transplants, and we've made major progress in fighting deadly illnesses like cancer and AIDS, yet we have made little progress in treating CFS. Greater research will help those of us with CFS but also help society at large when you consider the money spent each year on the treatment, care, and government aid to people with CFS. In the end, research is a win-win.

I am an optimistic person by nature. As a high school American history teacher, I tell young people how America is the land of opportunity where dreams can come true. I have dreams of my own. I want to get married someday, I want to get a PhD and become a full-time college professor. I've even dreamt of a career in politics. I've seen my friends all around move in the direction of their dreams and I want to do the same with mine, but for four years I've had to put my dreams on hold. Please help me and the hundreds of thousands like me who have CFS pursue our dreams. Please help us realize America's promise.

Carolyn, *California*
Accompanying Document: *Testimony by Carolyn.*

I have had CFS for 14 years after a bout of mono that evolved into CFS. I am currently a participant in the Stanford University valcyte trial. There are many distressing things about CFS. The worst is the incorrect assumption that it is not a real biologically-based disease. I dread having to say that I have CFS. It makes me feel embarrassed that I am whiny, lazy, or

faking it. Despite the CDC's recent public awareness campaign, we all know that this illness continues to be dismissed by many in the medical and scientific community. Scientists don't put much effort into research and insurers often deny disability claims. Colleagues, family, and friends invalidate or reject us sufferers, and few doctors will treat us CFS patients seriously.

Most patients feel abandoned, and CFS remains under-researched. My resulting anger and overwhelming desire to get well motivates me to get involved in advocacy efforts, although because I am worried about future job prospects, I am not comfortable revealing my full identity. Having an invisible illness along with a name that trivializes my condition doesn't help matters. If I walked with a limp or had a cast on my arm, things would be easier. To look at me, one would not suspect signs of illness. I am often told, "But you look just fine." The problem is, I am not just fine. People do not realize the almost constant amount of rest I had to get to reach a high enough level of functioning where I can leave the house so they can see me, nor do they realize this higher level of functioning is only temporary and quickly gets depleted and that more rest is required to replenish my exhausted reserves. Most would be surprised by the amount of time I spend resting in bed. This is not by choice but by necessity.

I know that it is hard for people to understand CFS and take it seriously. If I was not afflicted with it, I would probably have a hard time with it as well. The reality is that most people do not understand CFS. And why should they? In some ways, this aspect has been more painful than the illness itself. There are actions that can be taken to change the perception of CFS for me and for the million-plus others suffering from CFS.

Over the years, I have spent tens of thousands of dollars out of pocket trying to get well. I've tried almost every CFS protocol available, from taking numerous supplements and anti-virals to self-injecting heparin twice daily for six months. I eat a very restricted diet and have given alternative medicine a good run. A member of my support group jokes that he'd ride a tiny bike in a bear costume on Fifth Avenue if he thought it would heal him.

Dealing with medical professionals for the most part has been disappointing. In my quest to get well, I have encountered four types of doctors:

The traditionalist – This doctor does not believe CFS is a real disease or thinks that it's psychosomatic and that the patient is merely depressed. Treatments are psychological—anti-depressants, cognitive behavior therapy, and graded exercise is recommended. The majority of doctors fall within this category. These doctors are in desperate need of re-education.

The opportunist – This doctor looks at CFS patients and sees dollar signs. Excessive visits are scheduled, unnecessary and expensive tests are ordered, and the purchase of costly and numerous supplements specifically from the clinic are pushed. At one time my CFS support group was preyed upon by chiropractors and doctors who wanted to speak to the group and build up their practice. We now have a policy to not allow practitioners at our meetings because their intent is clearly opportunistic.

The sympathist – This doctor has some CFS patients, recognizes there is a real problem, but doesn't know what to do. Palliative care is provided.

The specialist – not many of these doctors exist. This doctor understands CFS, provides cutting-edge treatment options often not yet scientifically proven, and the practice is swamped. It can take over a year for a new patient to be seen. The doctor often faces ridicule from colleagues.

I recently asked top CFS doctors and researchers in the U.S. for their recommendations on what Congress needs to do on behalf of CFS. The recommendations of these doctors are provided below. While I urge my senators and congressman to act on these specific requests, I am also urging CFSAC to do so as well:

1. Increase funding for CFS research to at least double its current level.
2. Create at least five CFS Centers of Excellence each funded at $5 million a year.
3. Change the current NIH funding mechanisms.
4. Establish oversight of how the CDC spends its $4 million-plus annual funding.
5. Develop a national CFS registry.
6. Enact legislation to protect patients from unreasonable and malicious disability insurance carriers and provide resources for patients to better navigate the system.
7. Contact the Infectious Diseases Society of America to get an official statement or position that CFS is a real disease with potentially infectious ideologies and subsets.
8. Encourage all U.S. medical schools and primary care residency programs to include CFS in their curriculum and training programs. Require all primary care physicians to acquire one-time CME about CFS as a condition of renewing their medical license.
9. Recommend that the SG write and send a letter to health professionals including the Presidents of the American Medical Association and the American College of Physicians.

Sharon, Illinois

I am a long-term survivor of CFS. I was a practicing attorney primarily specializing in immigration law. I worked in California as assistant regional council for the Department of Justice before I became ill. I had a sudden onset of the illness and I had credibility, so I did not go through what a lot of CFS sufferers go through, which is a lot of months before a diagnosis.

I was diagnosed as having CMV [cytomegalovirus infection] and told to go home and get six weeks of complete bed rest. I had a very understanding supervisor at my Federal job because I was a very hard worker and in a high position. I couldn't stand up at all. The first couple of years of CFS are horrific. Whenever someone new comes to one of our support groups, you feel so bad for them because they can't even see through the tunnel at all.

I continued to try working, but I kept having horrible relapses where I was home for a month and a half at a time. I used up all of my leave, then had some advanced, etc. There's no way in the world that I wanted to stop being an immigration lawyer.

After a year and a half of trying to work with the illness, I went out on disability because I decided that I would rather go out sick than ruin my license. I couldn't understand what I was reading let alone brief my boss, who was going on Nightline later that day. So I stopped working.

That was in 1988. This is now 2008. I run into people I used to know and people are shocked that I'm still alive. The publicity campaign that has gone on in the last couple of years maybe is making an indent. However, on the medical side, there's still nowhere to go. I have a wonderful holistic homeopathic physician. She's an MD homeopath who has been treating me since I moved back to Chicago to be with my family.

I have detoxed and a lot of the detox does help, as it does with any viral illness. I got married and had a child—a child who had some special needs. She had a language delay. We live in fear every day now that she is 15 that she will get it as well. She has had to be raised by a mother who is disabled

The problem is that it is 20 years later and we're a little further relative to recognition, but we are no further relative to treatment, we are no further relative to knowing how it's transmitted, and nobody wants to deal with the contagion issue anymore, although it's out there.

Patricia Fero, Executive Director, *Wisconsin Chronic Fatigue Syndrome Association, Inc.*
Accompanying Documents: *Survey letter gauging interest of WCFSA members*
Documents depicting NIH funding patterns

When I started this 10 years ago, I was on the Internet trying to figure out what the mission statement was for CDC and NIH. I still don't get it—and I don't mean any disrespect at all—but here we are spending all of this time on CDC with the questions of etiology, diagnostic markers, and new meds and yet I don't understand why there is so much focus on the CDC, since NIH is the research agency. Do you think the CDC is going to look at etiology, and diagnostic markers, and new meds for whatever turns out to be CFS and the subgroups? I'm not so sure. I'd like someone to talk to me about that at some point, because I don't get it. It's a problem, and it may be indicative of the circular discussion that I was hearing this morning. Round and round and round, and we're not getting anywhere.

I had heard that there's some question about patient interest in CFSAC, and look at all of these people who have not testified. I sent out a letter about CFSAC to 216 members of the Wisconsin CFS Association. I got a return rate of 77 cards with all of these comments. People are tremendously interested, but, for example, there are CFS patients who are too sick to travel very far, and who have only two hours of up time. Out of the 77 responders, 68 individuals said that they would like to attend; 20 individuals said that the cost would be a factor; and 4 individuals said that they would not attend but that they would want some

information. Out of the 77 responders, only 5 individuals said that they are not interested in the committee.

There's a problem with communication. I'm seeing it right here, with not having enough time. These people want a video. I handed the 49 pages of minutes to someone who has been here to testify before and she said, "I can't process that." We need some way to communicate. This committee's important. Is there another way that we can communicate the importance of this committee and what goes on here to the population? If the clientele can't benefit from or participate in meetings, they will underestimate what goes on here.

Certainly those Wisconsin CFS Association members count. They're disabled. I want a calculation of what it would cost to somehow do a web stream or some other kind of alternative. Much of this constituency is silent and sick. Can they be heard in another way? Can they then apply pressure to their Congressional folks?

Dr. Oleske informed Ms. Fero that CFSAC has already looked into audio/video alternatives and that Dr. Parekh could discuss the details with her. Dr. Oleske said that a live web cast is prohibitively expensive.

Dr. Parekh responded to Ms. Fero's CDC/NIH concern by pointing out that CDC was discussed on Monday's agenda, but that NIH would be on Tuesday's schedule. He added that CFSAC is looking into different options for getting the meetings more broadly disseminated. Ms. Fero expressed appreciation for the thorough written minutes, noting that she had missed the November 2007 meeting, but could follow the discussion.

Marly Silverman, Founder, *P.A.N.D.O.R.A. [Patient Alliance for Neuroendocrineimmune Disorders Organization for Research and Advocacy], Florida*

Ms. Silverman called attention to the photos of CFS patients attached to empty chairs in the audience seating of the meeting room. Part of the Empty Chair Project, the photos are of people who wanted to attend the CFSAC meeting but were prevented from doing so by CFS.

She expressed appreciation for Dr. Parekh looking into meeting broadcasting alternatives, adding that many CFS patients currently feel abandoned.

She called the committee's attention to the fact that P.A.N.D.O.R.A. has sent a letter to members of the Congressional health appropriations committees. The letter was signed by P.A.N.D.O.R.A, the Vermont CFIDS Association, HOPE, the Wisconsin CFS Association, the Fibromyalgia Coalition International, the CFS and FM Organization of Georgia, and the New Jersey CFS Association. The organizations will do a follow-up letter inviting Congressional committee staffers to attend CFSAC meetings.

Ms. Silverman displayed for CFSAC members P.A.N.D.O.R.A.'s poster for the year with the theme, "Inspiring Hope Through Awareness." She noted that P.A.N.D.O.R.A. has declared May 12 Neuroendocrineimmune Disorders Day with the theme "One Voice, One Community,

One Cause" and a mission to support quality scientific research, quality medical treatments, and quality of life. She said that "I want to go to a NASCAR racetrack anywhere in the country and if I say I have CFS, you'll be able to understand what CFS means. Without CFSAC, I probably wouldn't be able to do that."

She continued on the subject of Centers of Excellence: "I don't care what you heard from someone else, they are very important. Without them we are not going to have the capability of really being able to do things like taking advantage of HRSA grants. There's nothing there. If we build, they will come. I know that there are budget considerations. I'm going through that in Florida. The College of Medicine at Florida International University is short $3 million because of a state budget shortfall. This means they're going to proceed on a much smaller scale and the possibility of us having the Florida Neuroendocrineimmune Center still remains, but it's going to double my amount of work knocking on doors saying that we need more money.

As far as the physician population, Rebecca made a powerful statement: there are doctors who know about CFS, but they don't want to treat us because we're too cumbersome within the five-minute framework that they have within insurance parameters. Since we don't have enough American doctors to take care of us, let's start recruiting from overseas. Right now we are mentoring a young physician from Colombia who has worked with Dr. Nancy Klimas and is at the University of Miami right now. We're going to be sending her to the HHV-6 symposium in June. I have filed two letters on her behalf with immigration authorities. They respond that we must prove that there are no American doctors wanting to do this job. Maybe you could figure out what it would take to bring doctors here. Young doctors are willing to do the work that American doctors don't want to do."

She concluded by announcing that P.A.N.D.O.R.A. is having a golf classic on May 23.

Dr. Oleske: The issue of doctors and nurses being recruited to come to the United States—the only issue you have to understand is that there are also CFS patients worldwide and sometimes we do a doctor/nurse drain that's not very fair because we are an attractive country in which to practice medicine. Yes, we want doctors here who can treat CFS, but we can't take all the doctors and nurses from overseas so that they don't have the doctors and nurses there. The same story has been going on with AIDS for a long time now. While I'm sympathetic, and there are individual doctors who trained here who want to stay and have the credentials to stay, we have to do a better job of educating our physicians in this country to take care of CFS.

Martha, Texas

I have ME [myalgic encephalomyelitis] and a host of other health problems too numerous to list. I ask that you read my entire written statement as I'm only presenting a shortened version. Prior to July 1999, I was a vibrant, healthy, happy, well-adjusted woman. I graduated with a BS in geophysics, and as a single mom I with a son, had a great career as a telesystems engineer with an annual salary of more than $70,000. I home-schooled my son, and was an active volunteer at church and Boy Scouts. Our hobbies included

catamaran sailing in the Gulf of Mexico, visiting museums, hiking, and fishing. After my sudden onset viral attack at the age of 38, I was bedridden. I was determined to get better, and rose from the ashes to recover 80 percent of my functionality.

Due to a relapse in 2003, caused in part by graded exercise, I now have 25 percent functionality. For a time we were homeless, living in the woods in a travel trailer without electricity. We got our water from a hose. The quality of my health is decreasing as each year passes. I am disgusted at the progress made in the nine years that I have been ill. Most of my recovery has been due to self-directed supplementation and experimentation after hours upon hours of research. I am disappointed by the new, ineffective CDC toolkit. I am deeply disgusted and offended at the information on the CDC website on CFS, specifically the theoretical and experimental test sections. This is shocking and surely must be a joke. It is clear that barriers are being created and the best interests of the ME community are not a priority of the CDC or the NIH.

I strongly urge this committee to represent the ME community as powerful and committed advocates for true scientific research that does not include a psychological focus. I would like to see the following five items:

1. Increased funding – there are far more people with the related invisible illnesses than there are HIV/AIDS patients, yet the funding ratios are reversed.
2. True scientific research – not one more penny should be spent on psychological studies.
3. Clinical trials – we need several randomized, double-blind, placebo-controlled clinical trials with lots of people in them. Those trials are now including only the most well among us.
4. The Canadian consensus document – I strongly urge this committee to block the CDC's efforts to align our government's policies regarding ME with the UK psychological attitude towards these related physical illnesses. The guidelines include post-exertional fatigue, a critical aspect of ME.
5. Change in criteria – we must move forward and accept ICD 10 and the Canadian Consensus document.

I am making this effort to speak to you today for two reasons:

- Myself – I have many good, productive years ahead of me. I am a young 46 years old and I desire to work and live free from pain and severe health issues. Please help me by exerting your influence as a committed and forceful advisory committee.
- My son—an Eagle Scout, a high school student attending the local community college, president of the Student Entrepreneurs, Phi Beta Kappa Honor Society, member of Habitat for Humanity and the computer club, recently voted new student leader of the year at the community college, and nominee and participant in the aerospace scholars program. He is exhibiting early warning signs of this illness. Please help my son fulfill his potential.

Dr. Oleske noted that Tuesday's agenda also includes public testimony from the CFS/ME community. **Dr. Parekh** added that CDC provided additional information for CFSAC members and the public about the research program.

Adjournment

Tuesday, May 6, 2008

Call to Order/Opening Remarks

Dr. Oleske called the meeting to order, expressing gratitude for the speakers' information and committee dialog from the day before and the support of Dr. Parekh and his office.

Roll Call/Housekeeping

Dr. Parekh took roll call, noting that Drs. Klimas, Reeves, and Desi were absent. Sarah Wiley sat in for Dr. Reeves.

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

National Institutes of Health and Food & Drug Administration Updates

Dr. Cheryl Kitt, Deputy Director, Center for Scientific Review, NIH

I wanted to talk about what is happening with our realignment of study sections, integrated review groups (IRGs) and divisions. We are not changing any study sections per se; if anything, we are adding new study sections. The reorganization is based on scientific alignments and information that we received from our internal reviews of all of the IRGs, which happened over the course of a year and a half. It was completed in October 2007 and we're about to start again in June with our IRG reviews.

We had six open houses, which concluded in December 2007. Some of the things that came out of the open houses include:

- We don't have a home for the review of translational and multi-component research. We are addressing that now.

- We initiated and received a lot of information about how neuroscience applications are reviewed. We had four review divisions where neuroscience was reviewed. We now have collated all the neuroscience study sections into one division called Neuroscience Development and Aging.

[Dr. Kitt presented a slide of her Center's organization including:]

- Four review divisions.
- 24 IRGs, each of which contain between six and 20 study sections.
- More than 250 study sections with more that 250 scientific review officers (SROs) running those study sections.

- This does not include the special emphasis panels (SEPs).
- We just added an IRG, which is in Emerging Technologies and Training in Neuroscience.
- We added the Neuroscience Division.

We have spent the last year thinking about where science is being reviewed and what kind of science is in the divisions and in the IRGs. We want to increase efficiency and effectiveness. We have big IRGs with only one IRG chief, and it's very difficult to manage people let alone science. That was one of the drivers.

We have a lot of people doing a lot of study sections, and they are all done a little bit differently. [Dr. Antonio Scarpa] and I try to visit every study section every year to pick up both best practices and inconsistent practices. We try to make changes as we go.

We have ongoing recruitment for SROs. If you or anyone you know is looking for a job at NIH, we have jobs.

Because of the reorganization and because of the increasing number of applications, we need more people to review them. We also have turnover. Between 10 and 20 percent of our staff does turn over every year because of retirements or career opportunities.

We have essentially reorganized the following divisions:

- **Division A** - Neuroscience Development and Aging – brings together for the first time all of the neuroscience study sections.
- **Division B** - AIDS, Behavioral, and Population Sciences – our Health of the Population IRG alone had 20 study sections and we really felt the need to split that, but its split along the lines will keep the clusters of study sections together.
- **Division C** - Basic and Integrative Biological Sciences – one may say that the majority of our applications are basic science, but that's a trend that seems to be changing. At least 60 percent of our applications are in the basic sciences, which will be split between Divisions C and…
- **Division D**, which is called Physiological and Pathological Sciences.
- **Division E** - Translational and Clinical Sciences. The CFS SEP is housed in the Musculoskeletal, Oral, and Skin Sciences IRG. Although the CFS SEP will be in a different division, applications will still go to the same person.

Dr. Oleske: There has been a lot of discussion about having reviewers who are familiar with what CFS is. When it falls under the Musculoskeletal, Oral, and Skin IRG, does that make it difficult for you to recruit people who would be aware of and have some background in CFS if they're going to be reviewing grants in dermatology and oral health? At least two of the three in the name don't fit.

Dr. Kitt: That placement was done before I got to CSR, but my understanding is that the original applications were put there because that's where the science of those applications was trending to be. Those applications were in those domains.

Dr. Hanna: The majority of fibromyalgia, temporomandibular joint disease (TMJD), and CFS--this is where they are reviewed. These are the same group of diseases that people are always trying to establish a common explanation for.

Dr. Hartz: One of the issues that the researchers have with the CFS SEP is that there are a lot of dentists who are reviewing our grants. There may be some overlap with TMJ, but it seems that we have people who are often not really qualified to review the grants.

Dr. Kitt: It's not a standing committee. It's a recurrent SEP. The members are put on based on the expertise that's needed considering the applications that come in.

Dr. Hanna: I know there's been this complaint about dentists, but I think if you look at some of the dentists who are included you will find that they are indeed pain experts. We have some amazing people who you are calling dentists who are really experts on pain who have done some really good science.

Dr. Kitt: The other issue is that when the applications come in they are based on science, but if they state CFS, they are mandated to go to this SEP.

Dr. Hartz: But if they're having other dental problems go to that, then there will be lots of reviewers on there who are…

Dr. Kitt: These only get CFS applications. There's nothing else in there. Occasionally there are scattered numbers of applications that may have CFS-related research in them, but they're very rare and very few and they may go to other study sections because the PI [primary investigator] has asked for that. We honor that request. If a PI asks for a study section, we grant it 95 percent of the time.

Dr. Glaser: This has been a particularly touchy problem because we have shown that over a two-year period, three different versions of the SEP had at the most 15 percent of the members with any backgrounds related to CFS. Because of that, there have been concerns raised about attracting people to support working on CFS and to submit their grants to that study section. It doesn't sound like this is changing. You were willing to consider having the societies provide a list of individuals who have the expertise to the SRO. We also talked about experimenting a little bit, so let me offer another experiment that you might think about. Why not expand the list of potential reviewers by asking people the names of three or four people who they think have the background to review their grant?

Dr. Kitt: We really can't take names from the applicants themselves. It's against NIH policy for fear of conflict of interest. If a program director gets a list of names to review, you can be sure they will not be used because it's impossible sometimes to detect what the relationship is to the PI. You can tell us who you don't want to review it. We have a national registry of reviewers that our SROs do use.

Dr. Hartz: The issue of credibility cuts both ways. The assumption is being made that the SRO will look at the list and actually try to find people from those lists to review. If the SRO chooses not to do that, you're right back where you started.

Dr. Kitt: They're required to look at the list. If they don't choose from the list, we ask them why they don't. We're very diligent about this. The other issue is that there is a limited pool of investigators who do CFS research. It isn't this untapped resource that people think we're not looking at. As soon as we see these applications coming in, we immediately start looking for reviewers who are the most relevant. If you can help us figure out another strategy, that would be great.

Dr. Hartz: It's very difficult for a number of reasons to have good reviewers for CFS grants. One of the reasons is that CFS is a hodge-podge. You can approach it 50 different ways and somebody who is appropriate for reviewing a part of one grant may be totally inappropriate for reviewing other grants or even other parts of a particular grant. I think it's going to be almost impossible to find reviewers who are necessarily suitable, and they have not been suitable. As someone who has submitted, I find much of the critique just foolish. Not that I disagree, I just think that the reviewers don't have a perspective that's useful. I wonder if there is the possibility of any kind of an appeals process so that if you feel that you have a review that is out in left field, there is a way that you can have other people brought in with different kinds of expertise.

Dr. Kitt: Yes and no. Yes, you can always appeal. The disadvantage to you is that you're not entitled to a revision at that point. You can ask for a re-review for inappropriate or lack of expertise or an unidentified conflict. The time to speak up is before the review. If you look at the roster (available 30 days before the meeting) and you feel you don't have sufficient expertise at that point, you immediately let the SRO know about it.

Dr. Jason: Thank you for coming back and for participating in the Research Subcommittee conference call. Based on the contacts that you gave us, the chair of the reviewer recruitment database did get a large list of names that the IACFS/ME and others put together and those have been entered into the registry.

You mentioned in the conference call several important and positive things for our committee to think about:

The SRO is retiring and that means there's going to be a replacement. Dr. Kitt said that she would be interested in getting nominations from us and the larger research community. The SRO is a key person in the process because he/she selects the reviewers. This is the time for our group as well as the CFIDS Association and IAFS/ME to be thinking about finding people to fit the bill—a researcher who has been out if the field and has some experience.

Dr. Kitt: The position opened May 1 and we have an open ad in USA Jobs. I'd be happy to talk to anyone who is interested.

This is a very brief window we have to be talking to Dr. Kitt and she has offered to have more interactions with our Research Subcommittee between now and the next CFSAC meeting. We should think about the possibilities of using this SEP to test out some possible different ways for review such as:

- Editorial reviews – a first round of reviews in which the panel states whether or not the grant should be scored. The second round would be a closer review.
- Getting feedback from people who are submitting grants as to their experience of the review process so that the information can be used to consider further changes.

Dr. Kitt: The most prominent thing that will happen as far as enhancing peer review activities is the shortening of the RO1 application to about 12 pages. Our task is to design what is in those pages as well as design and realign the criteria for review and the critique to ensure that the summary statements are not longer than the application.

We will be experimenting with editorial reviews in the near future. It's great to hear that you'd be interested. Lots of communities are interested, particularly small businesses. There are a lot of creative things that are going to be coming out in the next couple of weeks.

Review is always a challenge, and one of the challenges that I'll put back to you is how do you increase the scientific community to get interested in your problem? How do you get junior investigators interested in a problem that's almost intractable for them to even think about? The number of grants that NIH sees in CFS you can almost count on two hands. Why is that? That's what you need to take on.

Dr. Oleske: Why is it that someone who has been asked and volunteers to be on CFSAC is excluded from reviewing grants?

Dr. Kitt: It's related to the Federal Advisory Committee Act. It's a conflict of interest.

Public Comments

Jennifer, *Pennsylvania*
Accompanying Document: *Public Comments*

I sit before you in a wheelchair today because of CFS. I'm not here to tell you about all this illness has stolen from me or about the quality of the medical care that I've received. In fact if CFS was simply a medical problem, I wouldn't waste your time. But CFS is costing our country billions of dollars and is a significant health crisis. I am here to urge this committee to advise Secretary Michael Leavitt of the true scope of CFS and the burden of this illness. I am here to urge Secretary Leavitt to immediately direct his department to mount a meaningful response to CFS. The current level of investment in CFS research is not just inadequate, it is an embarrassment.

CFS costs an estimated $20,000 per patient per year in lost productivity and wages, according to a study published in 2004. The CDC's latest prevalence data estimates a patient population of 4 million, which means the impact of CFS on the U.S. economy is as high as $80 billion per year. That does not include healthcare or disability costs, so we can assume the true cost of CFS is much higher. The annual loss of $80 billion a year in productivity is a significant health problem. With all due respect to the agency representatives here today, your agencies clearly do not allocate resources on a scale commensurate with the problem.

Consider that lost productivity due to diabetes cost $58 billion in 2007. Last year, NIH spent just over $1 billion on diabetes research. In other words, NIH invested 1.7 cents for every productivity dollar lost. If NIH allocated research funds to CFS as it has to diabetes, then a 1.7 cent investment per dollar lost would translate into $1.3 billion dollars in annual research. Apparently NIH believes that CFS does not merit such investment. Last year the NIH spent only $4 million in CFS research—an investment of less than one one-hundredth of a penny for every productivity dollar lost.

Allow me to illustrate this gross disparity another way. There are 20.8 million Americans with diabetes. By spending $1 billion on diabetes research, NIH invested $48 per patient in 2007. In contrast, NIH's CFS research program represented an investment of one dollar per patient. It's well established that CFS patients are as disabled as patients with end-stage renal disease, multiple sclerosis, and AIDS. There is no treatment for CFS and doctors do not properly diagnose us. In contrast, diabetes can be effectively diagnosed and managed and doctors are quite familiar with how to educate their patients to maximize treatment efficacy. But NIH spent 48 times more money per patient on diabetes research than it has spent on CFS in 2007.

The CDC fares no better than NIH in this regard. While the CDC spent slightly more than NIH on CFS research last year, I must bring to your attention that the group published only two papers in 2007 and only one manuscript is in the pipeline this time. This is further evidence of the erosion of CDC's research program about which this committee has long been concerned.

Ladies and gentlemen, this situation is not acceptable. No reasonable person can be satisfied with claims that there is no more money available for CFS research. Money can be found for high priority problems. Our government is capable of addressing threats to our economy by bailing out endangered banks or flooding the market with economic stimulus checks. Yet here is a clearly documented cost to our economy of $80 billion in lost productivity each and every year, and the best NIH can do is spend a fraction of a penny for every dollar lost. This is foolish policy. Our economy needs 4 million CFS patients to return to their jobs, earn their salaries, support their families, and pay their taxes. If Secretary Leavitt has been unmoved by the suffering of patients and their families, then perhaps he can be convinced by the numbers. Do not tell me that we cannot afford more CFS research. The truth is we can not afford not to invest more in CFS research. And to answer Dr. Kitt's rhetorical question about increasing the number of applicants, if you build it, they will come. If there is money, they will apply.

You are obligated to advise the Secretary of the burdens of CFS, not just on individuals, but on the economy as well. You are obligated to tell the Secretary that the two agencies responsible for researching CFS and finding treatments for it saw fit to spend a tiny fraction of one penny for every productivity dollar lost last year. You must convince the Secretary that research spending should be made proportional to the size of the problem. I urge this committee to take whatever steps are necessary to secure meaningful action from the Secretary.

I have been ill for 4,962 days and I am waiting for this committee and the Secretary to act. And I do not wait alone. At least 4 million Americans and their families wait with me. I thank you for your attention.

Dr. Oleske: In your written statement, if you have a reference on the one penny per productive time lost, if that's published anywhere.

Jennifer: Those are my calculations based on publicly available numbers for research dollars spent, prevalence, etc.

Brian, *Nebraska*
Accompanying Document: *Written Testimony*

Although I may appear like a healthy young man to you, please be assured, I am not. CFS has stolen the last 13 years of my life and continues, on a daily basis, to deprive me of any semblance of a "normal" life.

Before I became ill with a severe case of mono during freshman soccer tryouts, I was a four-sport athlete, a 4.0 student, and a typical all-American 15 year old boy. During a time in my life that is developmentally vital, I spent over half of high school sick, in bed, with CFS. Not only did I miss out on the academic aspects of high school, but the important socialization that occurs with adolescence as well. I could not participate with my friends playing sports. I was too sick to attend Homecoming. I did not enjoy the luxury of having a high school sweetheart. This was not due to the inability to interact socially, nor the lack of desire to. This was due to the physical constraints that CFS placed upon me.

During my late teens and early twenties, it took nearly six years to achieve my Bachelor of Science degree. Not because I was the cliché undergrad, floundering along, afraid to enter the real world—but because I was forced to withdraw from classes and take lighter course loads, all because of the debilitating symptoms of CFS. Again, during a developmentally important time in my life, I did not have the liberty of participating in all the activities that young college students typically do. It was physically impossible for me to go on dates, to attend sporting events, or to go to college parties with my friends. Because of CFS, I was a prisoner in my own body.

Following college, I began working full time at a large investment company. In less than one year, I had suffered a full relapse of CFS and was forced to resign due to my disability. I

loved my work and would give anything to return to it. However, CFS has continued to ravage my mind and body, making this prospect an impossibility. I have aspirations of one day attending medical school. On the surface, I may appear as a sound candidate. I have satisfied all the major prerequisites, my GPA is solid, I have notable recommendations, etc. However, I must be a realist. The rigors of medical school would most certainly wreak havoc on my already CFS-weakened body, causing this dream to remain just that—a dream.

As a young American man, it is disheartening to not be able to participate in all the things that embody the American dream. I watch from the sidelines as my friends and peers embark on their careers, get married, purchase their first homes, begin families, etc. While my peers are afforded this luxury, I am relegated to living in my parents' basement. While most in my demographic are self sufficient, I am not and likely will never be. Make no mistake—this is not by choice. I want to work. I want to be successful. I want to one day have a family. I want to be a contributing member of society. I want all the things that CFS has deprived me of and has caused me to be a spectator to. But given the current state of my health as well as the inadequate response by the Federal government, these things remain unattainable and will likely remain that way—unless this committee, the DHHS, the NIH, as well as the CDC increase their efforts and treat CFS as the real and disabling disease that it is.

At the age of 24, I was diagnosed as being hypogonadal, secondary to CFS and likely the result of extended and frequent viral infection, according to my endocrinologist as well as my immunologist. As a twenty-something, I had to make the decision of beginning testosterone replacement therapy, which I am sure you realize is a life-long commitment. Many of you are also aware of the implications this decision can have on my ability to father children in the future in addition to the long-term consequences on my health.

I do not need to explain the mechanism of how testosterone replacement often terminates the male body's ability to perform spermatogenesis. However, I do need to explain how difficult and unnecessary a decision of that magnitude is for a young man at the age of 24. I do need to explain how difficult and unfair the decision to cryo-preserve semen is for a young man, at the age of 24. Please try to put yourself in my shoes. It is not easy to initiate a conversation with a potential girlfriend, explaining that due to CFS, I may never be able to father children. And even if a woman is able to overlook all of the other significant concerns that accompany CFS, breaching the topic of parenthood through in-vitro fertilization is colossal. I have had to make these choices. I have had to initiate these conversations. This is my reality. This is CFS.

Over the past 13 years, I have dealt with the myriad of symptoms that compose CFS. Beginning as a 15 year old, I have been force to navigate through high school, then college, with its layers of bureaucracy; the tangled mess of the American insurance complex; differing physician opinions; treatment options; etc.—all while being significantly disabled by CFS. I have a tackle box filled with medication. Just traveling here from Omaha, Nebraska, was a struggle, filled with airport pat-downs and searches, because of the medication that allows me some inkling of normalcy in a life otherwise plagued with CFS and all of the symptoms it entails. I have a three-inch thick binder that is filled with the past 13 years of my medical history. And please, lest you jump to the conclusion that depression is the cause of all of my

woes, know this—I am not depressed. I have been evaluated for depression on a number of occasions. I am frustrated—frustrated with my health, frustrated with the lack of treatment options, and frustrated with the government's inferior response to such a devastating illness.

This is my life. This is what CFS looks like.

Robert and Courtney, *Virginia*
Accompanying Documents: Written *Testimony*

Robert

I am here to tell my personal story of battling CFS for over 20 years. If I had not been able to participate in the Ampligen clinical trial, I would not be here today, with my wife Courtney, nor would I be able to interact with my eight year old boys, who are a great help to me.

It's not an easy statement for me to make that I am dependent on my two eight year old boys. I could do anything and was always the best at whatever I set my mind to do. I must now depend on my children.

I have always been an optimist and believed even early on, once diagnosed, that I would beat this illness and return to some degree of my old self. I put my belief in our medical technology and what I personally knew about our government's efforts to overcome chronic and terminal illnesses. It is now clear to me that the same government agencies that battle AIDS, cancers, and other life altering illnesses have retreated into hiding from CFS.

My family history of disease and involvement in clinical trials started over 45 years ago, when my younger identical twin sisters were born with a cancer called Wilms tumors. They were treated at Sloan Kettering Hospital. As infants, they each lost a kidney, removed with their tumors. My parents had made a choice in 1961 to allow doctors at Sloan to use experimental radiation and chemotherapy, which could either harm my sisters more or give them a few years of life.

There were 48 other children with Wilms tumors at the hospital then, and I'm sorry to say that my sisters were the only two participants in the new therapies and the only two who survived. My sisters never knew a normal life, but because of Sloan's dedication and my parents' willingness to participate, they did have life. One sister lived to be 30 and my other sister died at 40. I think, for cancer, Sloan Kettering represents the kind of Center of Excellence that we need for CFS.

Two years ago at the age of 49, my eldest brother died of cancer. He had been getting radiation treatments and chemo at Baptist Hospital for a germ cell tumor. He fought to stay alive for more than nine years. Not only did he benefit from radiation treatments that are now far more refined and less dangerous than when my sisters were young, but he received a combination of cutting edge chemotherapy drugs that gave him years more to live than predicted.

I have had CFS since the 1980s and I'll soon be 50. Before getting sick, I was a leader in my profession and an avid exerciser. Due to CFS, I was forced to change professions several times, trying to outmaneuver my illness. By the 90s, the illness had me bedridden and unable to work. I saw more than 30 doctors and specialists in that decade. I was told by one neurologist that the only way I could have the symptoms I described was if I had a tumor the size of a basketball in my brain. You've heard these stories before, how CFS patients don't fit mainstream practices.

Diagnosis is getting better, but treatment is not. CFS is a complex illness and that's why we need medical centers with doctors trained in CFS, dedicated to patient care, research, education, and clinical trials. We need Centers of Excellence for CFS.

CFS has weakened my immune system, so I am more susceptible to things like cancer on top of my family history. Only one medication is being tested in an FDA approved clinical trial—Ampligen, an immune modulator. Dr. Daniel Peterson, my doctor since 1997, enrolled me in the placebo-controlled study in 1999. At the end of the trial, the company gave all participants six months of Ampligen. Those last six months, I responded. I saw a glimpse of my old life. I was stronger, had more energy, and began to dream again. When that trial ended, I had a choice: to stop Ampligen or self-pay at a cost of $30,000 a year. Being the only treatment available, I had no choice.

I was on Ampligen for four years. Prior to Ampligen, my T-cell count was 369 and I was bedridden. During Ampligen, my T-cell count improved to over 1,000 and so did my physical and cognitive function. It was great to do some day-to-day activities that most people take for granted. Like pushing a stroller with my boys or sitting on the floor and having them crawl on me. I am grateful that I am one of the few people who had access to Ampligen treatment. I stopped the trial in 2003, thinking my immune system's strong response to Ampligen would sustain my improvements and because the costs were beyond us. I've now been off Ampligen four years and this year my health has declined.

Ampligen may not help all CFS patients, but if it can help some, that is success. It's the same way that some chemo drugs only work on certain cancers. We don't reject a cancer treatment because it only helps a subset of cancer patients. We battle cancer and HIV with multiple treatments and scores of trials. That's not being done for CFS.

The Federal agencies need to change everything about their approach to CFS. Patients need strong leadership, grant funding, clinical trials, and approved treatments from those responsible for our public health. Our health agencies cannot wait for the private sector to advance research and treatments on their own.

There are several researchers and doctors doing heroic work, some here on the committee, but they do it on almost no funding and they are overwhelmed. Nevada's moving forward with building an institute to address neuro-immune diseases such as CFS, Gulf War illness, MS, FM, and autism. Private funding got this started, but government funds will make progress faster. We need this project and other Centers of Excellence now.

More than 20 years have passed since the CDC went to Incline Village and yet no treatments have been approved for CFS; this is dismal state of affairs. Our Federal health agencies bear the responsibility for that disgrace. The time has come for change. I want to thank those here on the committee who are striving for a better path. You can count on seeing me again to support these bold initiatives.

In closing, look around you and give thanks, as we are all touched by medical advancements and clinical trials. But CFS patients have almost no access to clinical trials for our disease. My family has certainly benefited from cancer trials, and it has contributed to better cancer treatments for all. But without access to Ampligen and other clinical trials, I cannot be a productive member of society or a proper father to my sons. Real progress in CFS will only happen when our Federal health agencies decide it is time to focus on CFS the same way that it has with cancer and HIV. Imagine the possibilities.

Courtney

I wish I could say I am proud to be here. I am heartbroken. This is my husband and you've just heard part of his story. He and I are in this together. That's what our oath meant. But you need to know that the burden is great. Every year of paltry funding and squandered opportunities for our Federal agencies to lead us to discovery means years more before my family can hope for real recovery.

There is financial cost to this burden. Robert has worked since he was 15 years old. Now he's on disability. We have paid tens of thousands of dollars to participate in the only FDA-authorized trial for this illness. We paid for my husband to fly to Nevada to see his doctor, without whom there would be no path to understanding the very real deficiencies in his immune system that are making him so sick. We started to save for our twins' college education but had to stop. We have changed our residence to access expert care and we may have to move again because there are no experienced doctors who can help us through this maze.

The CDC says there are a million people in our nation with CFS. That's twice the number they said a few years ago and they say the average reduction in income is $20,000 to a CFS family. That's $20 billion in lost income and roughly $2 billion in lost Federal taxes if we simplify it. On a pure numbers basis, CFS is draining our nation and our economy.

But there is so much more to it than that. On the personal side, I measure the cost in what my twin sons miss. They are eight, and they have a father who is dedicated to their upbringing. But Dad can't play ball with them much these days. And we can't devote one-on-one time to our twins. When I'm not working, Bob needs the down time. Our sons bear the burden of this disease with him day after day.

We have actively taken on responsibility to advocate for more research and to enable clinical trials to improve patients' quality of life. We are among the privileged few who have found a doctor who has fought this illness with the tenacity, perseverance, and investigational skills that no patient can apply to their own health. The clinician/researchers on this panel need to know that you are our lifeline. Because you believe your patients are seriously ill; because

you believe there is one or more causes for their immune systems' breakdown; because you are collecting the samples, running the tests, finding the most curious scientists in relevant fields; because you are doing the work the CDC and the NIH should be doing, we are seeing slow but promising progress in the research. Dr. Bateman, Dr. Klimas, our own Dr. Peterson, Dr. Oleske, Dr. Snell, and others I have missed, you deserve more than we can ever give you in this lifetime for driving us toward discovery and treatment.

We are among the privileged few who could participate in the only FDA-approved clinical trial for CFS—Ampligen. You've heard the difference it made to my husband's immune system. He was able to care for our twin boys when they were younger. He was on Ampligen for almost four years and was able to sustain those improvements for three years after stopping it. The decline this year has been dramatic and reminiscent of the years before Ampligen.

I have to say at this point that there is no excuse for the length of time that Ampligen has been going through the FDA approval process. It has been 15 years. It is shamefully the only drug in trials, and it is not perfect for all patients. But it is critical for us, and many, many who are like my husband, and it's proven to work for them. The company that conducts these trials is not big pharma, it does not have an arsenal of paid consultants to grease the way, but it has the only patent for the only treatment that has shown improvement in CFS patients' lives with immune systems like my husband's. Yet FDA won't fast track it, won't approve it, and no other sizeable pharmaceutical companies will spend the money needed to investigate treatments for CFS. So we are caught in a Catch 22 the size of the Federal government. Only a few can get it at huge personal sacrifice and there are no other treatments in the pipeline.

While in Nevada we had the opportunity to lobby for a state bill to require insurance companies to pay for clinical trials in cancer. We helped organize our patient community to support it. We gave testimony, we got the provision passed, and we got it extended for clinical trials for CFS, a significant event for our community. My husband had ceased the Ampligen trial by then, but we did it because we knew it would create a good environment for trials. The success of that legislation created an enabling zone for clinical trials in that state which provided a foundation for the development of the Nevada Cancer Institute first, and now the Whittemore Peterson Institute for Neuro-Immune Diseases, like CFS.

I bring it up here because this is precisely the kind of public-private, interdisciplinary collaboration that our Federal health system should embrace and sponsor in our disease. It was launched by a large private gift which has been matched by critical contributions from the state and the University of Nevada medical school. Its mission is to advance patient care, research the pathophysiology of immune diseases, and develop therapeutics, diagnostics, and prevention strategies. It is an integrated approach by top researchers in different fields to unite patient care with research to find and cure my husband's disease. I believe our Federal health agencies should seed this institute with substantial funding to jump start this long-awaited change in approach to CFS.

I would urge this committee to pass a recommendation that this institute—our first Center of Excellence, if you'll allow me to use your phrase—be well-funded with grants and other direct

support. And I beseech this committee, make a recommendation to establish Centers of Excellence for CFS in a number of cities. Please do not let the agency representatives on this committee discourage you from making a recommendation that will spur change because it is too big and too much to hope for. They have been unwilling to change or hope for 20 years.

We personally get excited about the recent advances in genetic and viral science that a handful of doctors and researchers are leading. It is our hope for the future. But when I look at the budgets of the CDC and NIH allocated to investigating and researching CFS, I am appalled. Out of a $9 billion budget, the CDC only spends $5 million on CFS. The woman before us gave a great analysis of less than a hundredth of a penny; the NIH spends less. That's $10 per person with CFS. Let me go back to that $2 billion in lost tax revenue to the Federal government from patients. If you only look at dollars, you should want to spend $200 million a year to recoup $2 billion in annual tax revenue. You need to make that recommendation. We need you to think big, not small.

In closing, it's not news to me that my Federal health agencies don't respect CFS patients. That is the biggest reason that it has taken 20 years to make the advancements that are beginning to be made now. But it is unbecoming a nation that considers itself a leader in public health, in scientific discovery, in medical superiority. There are exciting discoveries to me made, but precious few scientists know that because the NIH and CDC won't fund them. They will tell me that we have to cry louder to get the money. I will respond: you have not banged the drums loudly enough inside your agencies, nor embraced the science aggressively enough in the scientific community to create the applications and you reject them when they come. The buck isn't big enough to pass around any more. And I really want to thank those on this committee who are struggling for real change.

Mary M. Schweitzer, PhD, *Delaware*
Accompanying Document: *Responses to the NICE Guidelines for ME and CFS by patient organizations in the UK* and *lists of tests the CDC insists that patients should* <u>not</u> *get*

NICE is Orwellian speak for what British socialized medicine has created to deal with CFS and ME. I don't think we have socialized medicine in the United States and my President tells us that if we did have socialized medicine, the result would be really poor care or no care at all. So I found myself astonished when I went to the CDC website and under "Treatment Options and Management Plans," headlined in bold, was a new sign right next to it declaring that the National Institute for Health and Clinical Excellence in the UK developed a new guideline to improve the diagnosis and management of CFS and ME.

It says that they worked with patients to get this. I'm telling you they did not, and these statements will show you they did not. The end of the story is that it was all once again an effort to say that the only thing to do with CFS patients is cognitive behavior therapy—which is the Full Employment Act for a certain kind of psychiatrist—and graded exercises therapy. As the CDC's own toolkit for professionals says, even with a bedridden patient like I was

when I had viral encephalitis, you can start with hand exercises and pretty soon you'll be up to taking care of yourself. If I did hand exercises, you wouldn't want to see them here.

I want you to look at this document on your own. The summary at the beginning is a good one and my personal favorites are the ones from the 25 percent group, which is a quarter of the people with ME who have the progressive form, which is what I had. I just kept getting worse and worse. Part of their testimony is that there were patients who were mobile who went through graded exercise treatment and ended up 25 percenters. They didn't become desperately ill until they went through graded exercise. If you put the studies together, the best conclusion you can come to is that there's a mildly statistically significant positive response in the short run, a lot of placebo effect, and not that much improvement in the long run. What's interesting is that they cooked the data. It is fascinating that even with a cooked data set, they didn't get much out of the study. And then you have all these serious adverse effects. If it was a drug, FDA would not approve it, and that is the point I want to make.

My CDC is saying this is great. Not the Canadian guidelines, which were written by a committee that included Nancy Klimas, a member of this group, and Dr. Dan Peterson, my own physician. CDC is advancing the guidelines from Great Britain, which were created so that they wouldn't have to pay for things. Those people over there can't get any of the tests that I had.

[Referred CFSAC to the second handout from the CDC website listing tests that CFS patients should not get.] I have Epstein-Barr, I think I have an enterovirus, we know I have HHV-6, I have a low natural killer cell count, I have NMH POTS [neurally mediated hypotension postural orthostatic tachycardia syndrome] but you're not supposed to give those tests, so I wouldn't know this if I hadn't gone to doctors who understand the disease. My question is this: we are expressly not in socialized medicine here, so who is the CDC talking to, really, when they say don't give us these tests? They are not talking to the public. They are talking to physicians who get reimbursed by insurance companies. They're talking to disability insurance companies. The point here is if you follow these guidelines, you have a circular reasoning that patients with CFS don't have anything. So we end up with the same thing that we had before.

Peter White, who I believe has been involved with a lot of studies that CDC has done on CFS, gave a talk last week in London where he said the CDC's criteria for CFS do not work. He said don't use the CDC guidelines, use the NICE guidelines or the Oxford guidelines for CFS (which say there are no symptoms). NIH does have a reference to the Canadian document and they do have a page of definitions that are at least neutral.

I want you to read what has been said about the NICE guidelines. There are seriously flawed and they do not belong in the United States. We don't have socialized medicine, the last I heard.

The last thing I want to say relates to the guy who was up here. Last time I talked to you, I told you what would happen if I lost Ampligen. I lost it two months ago. The clock is ticking—I got 10 months to go.

Meghan-Morgan Shannon, *Pennsylvania*
Accompanying Document: *HHS CFS Advisory Committee testimony*

What I am going to say does not apply to you [CFSAC]. A weird thing happened in that 12 years ago, I presented before Dr. Lee on the CFSCC committee. I want to read something that is still relevant today. This was April 10, 1996. I was co-coordinator for medical professionals with CFIDS/ME, founding member of the North Coast San Diego Support Group and also the Southwest contact for Rescind.

The part that I want you to read—now you're getting the whole speech, because it has mysteriously disappeared out of the record—is a "request for Congressional investigation into the CDC, NIAID, NIH, and Children's Hospital San Diego." I was requesting an investigation into the misappropriation of funds. This was April 1996.

The second request—and it also came from Congressman Nadler's office because he opened Congress four days later with the same thing—was a request that [the late] Dr. Steven Strauss of NIAID and Dr. Reeves of CDC be removed from their posts as of that day. "These two doctors have blatantly abused their positions of high office to impede any kind of adequate research and care for the population of disabled people with CFIDS/CFS." ME was not in the picture that much yet. "Their actions and words go way beyond ignorance and disbelief of this disease. It has moved into malicious intent to slander a population of disabled people." You can read the rest of this. I did this because I was asked to present this by Congressman Nadler's office. He followed it up, opening Congress with this same request. That's 12 years ago.

Briefly who am I … I am a long-standing patient advocate who started the North Coast San Diego CFIDS support group. Eleven women—we sat in a room together in 1985. I was a respiratory therapist in a cluster outbreak of Adeno Virus #2 from 1980-1983 when the infectious disease doctor for the workers at the hospital told me to leave, as my immune system was shot. It actually mimicked AIDS. The CD4/CD8 ratio was totally reversed. That is actually true for anybody who has polio. They're finding this out now. They didn't know this then.

I was first diagnosed with ARQ in 1985 by Dr. Allan McCutchen a very well-known AIDS doctor at UC San Diego. Then in 1988, I suddenly became an hysterical woman because you had to have HIV positive to have ARQ, and then came the CFS definition. They all happened in 1988. So I was legitimately ill and I became an hysterical woman in less than 24 hours. In 1998 I was correctly diagnosed with post-polio in England by the late Dr. John Richardson.

Most symptoms were overlooked yesterday in this committee by the CDC and NIH. Cardiac problems are big. There are some people in this room who will say yes, it's a huge problem. I have blood pressure and pulse that bottoms out together. That's not the way it's supposed to go. Normal saline takes me out. I wear a bracelet, I have a port. If I pass out on you, do not give me normal saline, give me Lactated Ringers. Fatigue is a factor in NMH POTS

(neurally mediated hypotension positional orthostatic tachycardia syndrome) and can be helped by medicine. CFS is a misdiagnosis of diseases. CFS is not the name of a disease. We've got to keep getting it out. CFS and CFIDS are names that are misdiagnoses of disease processes that may not have yet been discovered in patients who have been mislabeled with these names. I is the correct term for those who have this.

I am a classic misdiagnosed person. I have post polio. The late Dr. Judy Morris had MS when she took her life two months ago. She was ER doctor. If this doesn't bring this home to you medical doctors and clinicians—it could have been you. I was a very well, active, respiratory therapist at Children's Hospital. I was taking care of newborns who weighed less than a pound and we didn't have the respirators at that time. We had to calculate everything we were doing. So, I hope it comes home to you and I think it does.

- The names CFS, CFIDS, and NEIDS are not real names of diseases. These are acronyms and symptoms and body systems. Real disease processes are cancer, AIDS, Bell's palsy, MS, lupus, arthritis, etc. In 1994, Dr. Philip R. Lee, Assistant Secretary of HHS, stated, "CFS was never meant to be the name of a 'new' disease. It was to be a research definition for a surveillance study at CDC, and NIH would do testing for what was this outbreak of diseases."

- Epstein Barr and other herpes viruses are known to be latent. Studies in the UK, Europe, and other parts of the world are now looking at the fact that if you test for EBV and some other herpes viruses (not HHV-6), that these other herpes viruses are what is left behind after some other microbe or environmental insult has done damage to the body. I hope you hear that—the EBV is showing up in many diseases as "causes" and it may be just showing up because it's left behind and the immune system is down.

- Work incentive—the SSA people were very good. They were not doing this, but there were shades of being in the UNUM insurance meeting that I was in that the goal was to get people off the support they need that are disabled. UNUM is straining SSA and other agencies. The goal is to get sick people back into the mainstream making money. That is their one and only goal and they are training SSA people. SSA is not really taking this tactic. I have been out of my profession for 20 years. I don't think you want me back in Children's Hospital working with highly sick respiratory kids.

  What UNUM was saying is get us into anything—stuffing envelopes. That's what I'm afraid might happen here with Social Security. I know they're trying to take care of us and do something, but this should not be a government agency-driven thing to get me back to work. This should be between me, my doctor, my family, and my friends. This should be my decision, not a government suggestion. Help me, but do not say that I have to get back to work.

- CDC should not be allowed to control this disease. It's not in their mission statement. NIH should not be either.

- There are needs for Centers. We cannot have just one. The CDC in Atlanta is in the Southeast of the USA. Washington, DC, runs our government. We can't have a Beltway for this disease. We need four or five throughout the United States. You don't have to get Centers through this committee. CFSAC can recommend and then separate people can come to Congress to testify. We were on that track of getting well-recognized in April of 1991. So we can do this without going through this committee.

- SSRIs (selective serotonin reuptake inhibitors) should not be allowed in the country. They flood the brain with serotonin and cause major problems including violence and suicide.

[Ms. Shannon cited a passage from the latest edition of *Our Bodies, Ourselves* on CFIDS/ME that states that it is not a rare disorder and that "reaction to this epidemic has revealed many inadequacies and prejudices of the U.S. health care system, particularly fears of 'hysterical women.'" She noted that the disease is minimized as "Yuppie Flu" or an illness of middle and upper class white women even though Latinos and African Americans appear to be disproportionately affected.]

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

Office of the Surgeon General – Provider Education

Mary Beth Bigley, Senior Science Advisor, *Office of the Surgeon General (OSG)*

[Dr. Parekh noted that the Surgeon General (SG) has been receptive to CFSAC recommendations and understands the gravity of a diagnosis of CFS.]

About a year ago the recommendation went forward that the SG sign a letter to raise awareness among health professionals for CFS. We've been working for the past year to determine what the status of the letter would be. The SG realizes that this is an important public health issue and recognizes all of the other disability and employment issues raised by CFS. We also realize that the healthcare providers need this information so that they can make appropriate and timely diagnoses, management, and treatment.

As we looked at what would go forward from the SG out to the health providers for this awareness, one of the things that we considered was, what has the SG signed in the past and sent out to providers? The letters that we supported in the past have been from the documents that have been published through the OSG. The OSG has not published any document, call to action, or report on CFS nor have we had a workshop on CFS. It was determined that we would not be able to support a letter such as this because the information has not been generated through the OSG.

OSG Publication Levels

1. **Concept paper** – When a public health topic is brought to the OSG, there's usually a concept paper written to explain what the problem is and the impact of the problem. At that point, there's usually a discussion of having a **workshop**. A workshop brings in experts on the topic area such as researchers and epidemiologists to discuss what we know about the topic area and what the knowledge gaps are. The information that's brought to the workshop determines the level of scientific evidence around the public health topic area to see if there's enough information to then generate a Call to Action.

2. **Call to Action** – An evidence-based scientific document that outlines the issue and determines the stakeholders involved. The Call to Action also lists recommendations about how each stakeholder could continue its efforts towards adding more information to the topic area. A scientific body of evidence usually exists from which an SG's report can be generated.

3. **SG's Report** – A document full of concrete, evidence-based science and physiology concerning the health topic. The most recent SG's report was on second hand smoke.

The last letter that was sent from the SG pulled out a chapter on children from the second hand smoke report. It was sent out to providers in conjunction with the family practice organization stating the importance of the second hand smoke issue to the health of children.

Committee Discussion

Dr. Jason discussed the important public health effects of the documents coming out of the OSG, citing how the report on tobacco in the 1960s was a public health turning point. He said the message from the preceding group of public testifiers is that there are literally hundreds of thousands of people in this country who are some combination of unidentified, extremely sick, and not part of the current healthcare system. He asked if that kind of testimony along with supporting data would warrant a workshop and if not, what could CFSAC do to make a CFS workshop occur?

Ms. Bigley said that she and the OSG recognize CFS as a large public health issue that has a lot of variables. She said that she thinks that CFS could be a workshop topic because there is enough information to define the problem, but significant knowledge gaps exist as well. She said that a workshop would pull that together what is known and help to determine an action plan on what the next steps should be. She suggested that CFSAC work with the other HHS agencies, including CDC and NIH, to develop a concept paper for the SG to consider for a workshop. She referred CFSAC members to the SG's website to view proceedings of past workshops, including those on health literacy, healthy homes, and deep vein thrombosis. She said that workshops bring attention to public health issues.

Ms. Healy brought up the previous day's discussion of AHEC as a vehicle for distributing a letter similar to the one that was being drafted for the SG that would tell providers about available CFS resources. She asked whether the SG could send out such a letter internally

to reach AHEC grantees, HRSA, or wherever else clinicians are in the Federal system. She also asked whether Ms. Bigley had any other suggestions on getting the information out other than through a workshop.

Ms. Bigley said that she would take the idea back to the OSG. She repeated, however, that the OSG has generated letters that have come from internal SG documents and since none have been done on CFS, the Public Affairs Office will probably say that such letters would have to come from the heads of the agencies overseeing the grantees.

Dr. Oleske recalled from his AIDS experience that when Surgeon General Everett Koop attended a two-day meeting in Philadelphia on the disease, it was a dramatic statement. When the report came out from the SG on women and children with HIV, it was the first time that governmental agencies recognized the problem. It was a watershed moment, and it moved the field dramatically. It eventually led to the prevention of transmission from mothers to children. Dr. Oleske said that the current SG could do the same for CFS. He said that the prestige and authority of a report from the SG would be even more powerful than a letter. He emphasized that CFS patients and the providers who treat them have a sense of urgency that they do not see outside the field.

Dr. Jason asked whether it would be appropriate to move that CFSAC wants to continue negotiating with the OSG, recommends a workshop, and will do everything possible to provide materials in support. Dr. Oleske suggested that the motion be left for committee discussion. Dr. Papernik confirmed the order of actions leading up to an SG report:

- A concept paper from CDC/NIH and others on the epidemiological, economic, and other impacts of CFS.
- A workshop of experts around the country to give the SG a level of evidence for a Call to Action letter.

Ms. Bigley noted that although the SG hosts the workshop, the concerned agencies that drew up the concept paper would pay for the workshop. She recommended that CFSAC work with interested agencies to build a concept paper. The agencies would brief the SG on what they want a workshop to look like.

Mr. Newfield wondered whether there may be opportunities to coordinate the CDC external review panel information with efforts to develop an SG workshop. **Dr. Hanna** remarked that CDC/NIH approval for involvement in an SG workshop would come from the Director level, not from her or Dr. Reeves. **Dr. Snell** suggested that a request to agencies to produce a concept paper might have to come from the HHS Secretary because CFSAC does not have a mandate to make such requests. **Dr. Willis-Fillinger** asked Ms. Bigley to provide CFSAC with an idea of how workshop information will be eventually used. Ms. Bigley responded that workshops can be designed to deliver the results that the sponsors want to see based on the information they go in with. Many times the workshops produce action items that can be used as a platform for further policy development and research funding.

New Jersey Medical Student Scholarship Presentation

Dr. Kenneth Friedman, Associate Professor at the Department of Pharmacology and Physiology, *New Jersey Medical School*
Accompanying Documents: *Chronic Fatigue Syndrome Medical Student Scholarships New Jersey Chronic Fatigue Syndrome Association Medical Student Scholarship Program Winning Essay, Uma R. Phatak, Class of 2009, New Jersey Medical School*

Dr. Oleske introduced Dr. Friedman as a colleague of 30 years, one of his former professors, the father of a CFS patient, a former CFSAC member who helped guide the committee in its early stages, and an active participant in the New Jersey CFS Association (NJCFSA).

Dr. Friedman

My daughter got CFS at 17. She is now 33 years of age and she is coming to the point where she will have lived her life as much with CFS as without it, a sad moment because I thought I would be able to help her.

Dr. Friedman provided a brief history of his work experiences to demonstrate his expertise and knowledge about the topic of CFS.

Professional Affiliations:

- Board member and Chair of the Membership Committee, IACFS/ME
- Board member and Chair of the Medical Student Scholarship Committee, New Jersey CFS Association
- Secretary and Chairman of the Public Policy Committee, P.A.N.D.O.R.A.
- Member, Vermont CFIDS Association

Consultant service:

- MedaCorp, a private banking group trying to raise venture capital for private companies. I advise companies over the phone without knowing who they are.
- Hemispherex – consultancy limited to public policy and information on the needs of CFS patients, not drug development.
- Pfizer – consultancy limited to public policy and information on the needs of FM patients, not drug development.

He then proceeded with his presentation on the NJCFSA Medical Student Scholarship Program. The medical student scholarship program is the idea of a vice president and board member of NJCFSA, Betty McConnell. She also had the idea to develop a scholarship for high school CFS patients who want to go on to college. I was asked to implement the medical student program.

In New Jersey as elsewhere, there is an inability of patients to be diagnosed and treated for CFS. Even I, as a medical school professor, had difficulty getting my daughter diagnosed with CFS. I knew within six months what she had, but to get an official diagnosis from a clinician willing to make a diagnosis took about two years. This was despite the fact that my daughter did rotate through the New Jersey Medical School and the university hospital at the place where I worked, the University of Medicine and Dentistry of New Jersey, which advertises itself as the largest freestanding U.S. medical institution.

I was incensed that my daughter took so long to be diagnosed, and so I requested that CFS be included in the curriculum of my own medical school. My request was rejected with the statement that if syndromes like CFS were included in medical school curriculum, there would be such a flood of other similar conditions that would need to be included that the curriculum would be overwhelmed.

Having been rejected by my own school, I decided to try to figure out what was being done in other medical schools by writing organizations such as the American Medical Association (AMA) and the American Association of Medical Colleges (AAMC). My requests were rejected. During my appointment as a CFSAC member, I served on the Education Subcommittee. The subcommittee sent a similar letter to the same two organizations with the same result; neither organization would respond to the subcommittee's letter of inquiry.

Design of the NJCFSA Medical Student Scholarship Program

- The intent of our program is to supplement rather than compete with the medical school program. We will not gain anything by having a confrontational relationship with medical schools.
- What we are doing in NJ is the first of its kind: stimulate medical student knowledge of CFS, an illness that is not covered by medical school curricula.
- Only rising second year students are eligible. This is because the summer between the first and second year of medical school is the only one during which a student is not engaged in course work.
- All three medical schools in NJ are under the umbrella of the University of Medicine and Dentistry, so every medical student in the state has the opportunity to apply for the scholarship to learn about CFS and be compensated for that learning.
- Applicants write an essay on an assigned CFS-related topic.
- The assigned CFS-related topic changes yearly so that new applicants cannot rely on the efforts of those from previous years.
- The application process must be completed by the beginning of the second year of medical school to avoid interfering with the curriculum.
- A committee selects the best essay based on the criteria of scholarship and organization, and the winner becomes the NJCFSA CFS Medical Student Scholar.
- The scholarship pays $3,000 of the tuition remittance, $1,500 per semester.

Administration of the Program

- Our scholarship program is being administered through the Foundation of the UMDNJ, a private foundation with the goal of assisting the university with worthy projects.
- The program needs an endowment of $60,000 to yield a $3,000 scholarship per year.
- NJCFSA has committed to raising that money. We're in the process of doing that now.
- NJCFSA has agreed to contribute a minimum of $1,000 per year for the endowment fund.
- While we are raising the endowment, we are continuing to give the $3,000 per year for the scholarship from our annual income.

[Dr. Friedman played a DVD of the program's two scholarship winners' speeches.]

There is now an expansion of the Medical Student Scholarship Program courtesy of P.A.N.D.O.R.A. There are going to be two new additional CFS Medical Student Scholarships:

The Nancy Klimas Award

- Potential value of $2,000.
- To be given to a worthwhile medical professional organization for a scholarship geared to medical students and/or junior researchers.
- Plans for how the grant is to be distributed are still being finalized.

The Dr. Kenneth Friedman Award

- A five-year medical student scholarship to the Vermont CFIDS Association with whom I have worked for the last five or six years.
- There will be a $1,000 outright gift for a scholarship for the first two years.
- Vermont CFIDSA will be asked to fund $250 of that scholarship for the third year.
- Vermont CFIDSA will be asked to fund $500 the fourth year.
- Vermont CFIDSA will fund $750 the fifth year.

The intent is for the organization to be able to develop the financial resources to support the scholarship on its own. At the end of the fifth year, we believe that Vermont CFIDSA will be able to support the scholarship and if not, P.A.N.D.O.R.A. has pledged to review the circumstances and perhaps reinstitute the scholarship for a second cycle.

The big question, is can CFSAC recommend a national medical student scholarship program to the Secretary of Health? I think the answer is yes based upon the fact that DHHS currently has six health profession training scholarship programs:

- A year-off training program for graduate or medical students to spend the year at NIH engaged in biomedical research, after which they return to their degree-granting

program. It would be possible to rotate a medical student through NIH and give him/her an experience about diagnosing CFS.

- The National Health Service Corps Scholarship, which pays full tuition and fees plus a monthly stipend. The recipient is obligated to practice in a Federally-designated, high-priority health manpower shortage area for each year of support. I would classify CFS as qualifying to meet that need.

- Commissioned Officer Student Training and Extern Program (COSTEP) - Junior COSTEP option – for students who have completed at least one year of medical, dental, or veterinary school. The students work in Federal agencies for 31 to 120 days. Most students are hired to work in the summer. A medical student could work at NIH or another agency that could provide experience in dealing with CFS.

- Senior COSTEP option – for students who have at least eight more months remaining in their school career in medical, dental, nursing, pharmacy, and physical therapy. Scholars agree to work for the Commissioned Corps upon graduation. There is a service obligation equal to twice the time sponsored. Here again is an opportunity for students to learn about CFS by working in a facility that treats it.

- Clinical/Research Electives for qualified medical and dental students. NIH has short-term clinical rotations and research electives, so I believe that it would be possible to rotate medical students through this kind of program.

- Clinical Research Training Program – a 12-month intramural program at NIH for medical or dental students who spend a year engaged in mentored clinical or translational research. I think that this would be something that would be amenable to a CFS program.

Dr. Friedman closed by inviting CFSAC members to a May 12 screening of a film documentary about CFS called “Invisible in Vermont” produced by Exile Media, which also produced the scholarship awardees DVD.

Dr. Jason noted that with some negotiation with program administrators, the scholarship award programs may be able to be listed on the website of IACFS/ME. He also asked Dr. Friedman if CFSAC has ever asked the HHS Secretary to request CFS curriculum data from medical schools. Dr. Friedman replied that he had not, but that it should be pursued. If there are enough scholarships and if CFSAC can get a Federal scholarship program going, the AMA and AAMC may rethink their position on whether CFS should be included. **Dr. Snell** suggested that a CFS scholarship awardee be invited to speak before CFSAC about what difference the award has made to him/her.

Dr. Oleske noted that there is a move among medical schools to introduce into the curricula a resurgence of humanism in medicine. He has told his medical school that CFS is an ideal disease to emphasize this need. He said that Dr. Friedman’s work will influence the improvement of the care that CFS patients receive and of research in the field by stimulating

the next generation. Dr. Oleske said that most physicians will practice what they were taught in residency and if they were not taught it, they're not going to learn new tricks. Introducing CFS and the concept of humanism in medicine to medical students may be creating the greatest allies in coming to grips with CFS.

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

Dr. Cavaille-Coll explained that his division is one of two that are involved in reviewing products for CFS. He said that the FDA continues to implement the measures that were included in the FDA Amendment Act of 2007, which was an important turn for the agency. The act continues many of the important things that have been implemented in the past and has given new responsibilities and resources:

- There is a big emphasis on drug and food safety.
- The Critical Path Initiative is in place to find novel ways of developing products with an emphasis on biomarkers.
- A program for validation of biomarkers is running in the Center for Drug Evaluation and Research.

In addition:

- FDA continues to consolidate its campus at White Oak, which will eventually result in a much more united group.
- The FDA's website is being constantly improved to reflect the various new measures that the Act requires.
- There is no longer a link to FDA on the CFSAC website. Dr. Cavaille-Coll said that he will be speaking with the Office of Special Health Issues to determine the appropriate link.

Committee Discussion

Ms. Artman: Would it be possible for the CFSAC website to link to the statement that FDA employees cannot comment on ongoing trials? CFS patients are concerned about Ampligen, and it would be good for them to know before they pursue information that FDA staff cannot comment.

Dr. Cavaille-Coll: I will bring that up with the Office of Special Health Issues. It is a matter of law and a frequent question. I will pursue how it can be better addressed.

Dr. Jason: Two articulate CFS patients testified about their struggles to maintain their identities and health in the face of losing access to Ampligen. Given their powerful testimonies, I would think that we as a group have some responsibility to those who are suffering without Ampligen. I don't know what more we can do, but I think we need to take

action. Do you have any suggestions as to what we can do? This situation is at the point of a crisis.

Dr. Cavaille-Coll: I regret that I cannot comment on the status of any application that is under review. That is part of criminal law. Drug development is done by the companies. They must initiate it. We cannot design and fund the studies. We can help them by advising them how to develop a successful Investigational New Drug Application to allow a new molecular entity to be tested for the first time on human subjects. We will meet with them about our review results and next steps to take. The FDA website details the steps in drug development.

We're really in a difficult position with CFS because unlike many other diseases, we don't have an invitro model or an animal model that would allow us to select out of the thousands of molecules which ones could be worthwhile developing.

Dr. Jason: In the HIV/AIDS field when patients were discontent with the time it was taking to get drugs onto the market, it seemed like the FDA was able to respond differently. Was that a reality, and what can we do to facilitate that happening in this field?

Dr. Cavaille-Coll: I began my career studying HIV even before the virus was identified. I joined the FDA in 1990 in the Division of Antiviral Drug Products and I was there to see how everything changed in how we approve drugs. That was the time during which we developed the concept of accelerated approval. This acceleration took place once HIV was identified. A large part of the subsequent success was an understanding of the etiology.

Dr. Bateman: Ampligen is currently available through an open label study. If it is not approved by FDA, will patients continue to have access to this drug?

Dr. Cavaille-Coll: That's not a question that I can answer. Companies have to decide whether they want to make a drug available. That's a business decision. The FDA has different ways of making drugs available while they're under development and this is the one that was chosen for Ampligen.

Dr. Snell: It's over two years since the double-blind study on Ampligen was completed and there's still been no peer review publications on the study. That doesn't help the scientific community make a judgment about the efficacy of the drug or even CFSAC make recommendations for or against the drug.

Nancy McGrory-Richardson, a public and physician education manager for Hemispherex, the company that is developing Ampligen, noted that the company has submitted a study article for peer review and that it is "very close" to being published.

Dr. Eleanor Hanna, Associate Director for Special Projects and Centers, *NIH Office of Research on Women's Health (ORWH)*
Accompanying Document: *Information folder on the NIH Grantsmanship*

Workshop for Research on CFS

Dr. Hanna noted that the NIH grantsmanship meeting was videotaped and is available on the agency's website. She said that one goal of the workshop was to make people aware of K grants and T awards so that people know about mentored career advancement awards and the opportunity to develop teaching programs in CFS. The folder also included abstracts of NIH-funded research. She said that CFSAC members could consider asking some of the researchers to present to the committee or request that she invite intramural scientists to appear. Although they may not focus specifically on CFS, they have made many of the discoveries that are the backbone of CFS research.

Dr. Hanna also reminded CFSAC members of the Promise Initiative that comes out of the NIH Roadmap in which researchers are developing validated instruments to measure many of the health conditions associated with CFS, including fatigue.

She informed the committee of several recent or upcoming events:

- The National Institute of Mental Health (NIMH) re-released its co-morbidities funding announcement. NIMH is willing to look at CFS in relation to any mental disorder, meaning a researcher could study the difference between CFS and depression or any other mental health issue.

- The National Institute on Aging (NIA) and ORWH recently announced funding for a study of fatigue and aging.

- The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is sponsoring a meeting in June 2008 on its map initiative on chronic pelvic pain that will bring together investigators and hopefully announce who has received funding.

- Also in June the Temporomandibular Joint and Muscle Disorders (TMJD) Association is having a meeting that will bring together experts on CFS, FM, TMJD, and a number of other conditions.

- On June 20, 2008, Dr. Hanna's working group will hold a meeting of the PIs who were successful in competing for the CFS RFA in 2006 in order for them to present their results. Dr. Hanna's office will encourage them to form a collaborative so that they can conduct more extensive research.

- The Foundation of NIH has contacted Dr. Hanna for a recommendation on donor funding of CFS. She made several recommendations and requested a meeting to discuss an intramural fellowship for CFS through the foundation. She was scheduled to meet at the end of May to explore the subject and has commitments from two NIH staff to be the intramural investigators to help start up the fellowship.

Committee Discussion

Dr. Jason: Pat Fero has provided a report to CFSAC on the number of CFS grants that have been funded at NIH:

2001 – 4
2002 – 0
2003 – 3
2004 – 1
2005 – 2
2006 – 6 (with the RFA)
2007 – 3

Given the enormity of the issues that we're faced with, how do we get more grants submitted and funded? If this were another field such as HIV/AIDS, this would not be acceptable.

Dr. Hanna: I don't think that we find it acceptable for CFS either, which is why we've been working so hard to try to increase interest among scientists. These statistics talk about new awards each year, so you're forgetting that there's a backlog of renewed awards. People focus a lot on the money that's been issued and there are mistakes in those dollars figures. The actual money expended is probably between her lowest amount and her highest amount.

But that's not the issue. I think the issue is what we try to do to interest people. We can only do so much. We will be having a meeting within the next two years on which we might base an RFA. But there are opportunities there for people to apply to and I'll have to echo what Cheryl said. A lot of it is up to your organizations to encourage your members to take advantage of the many funding opportunities that are available to them, especially in times of tight money. I know that the President finds money for what he wants to fund—money that isn't there. But the agencies are not able to do that. There is no appropriation for CFS research. The budget is what it is. What research we fund depends on what research you submit to us which we try to encourage with the RFAs and program announcements and by doing the work we all do together at the NIH.

Dr. Hartz: There are some researchers in CFS who believe they have submitted good grants and these grants have not been appropriately reviewed. The response that I heard this morning from Dr. Kitt was that we're doing a good job. Reviewing CFS grants is not the same as reviewing grants for well-defined conditions. It requires a different approach because it's very difficult to find reviewers who are going to understand various approaches, sometimes within one grant. It's discouraging to feel like you've written a good grant and then to have the comments come back that don't make sense. One way to increase applications for CFS grants would be for people who are submitting those grants to feel like they've been fairly reviewed.

Dr. Hanna: The success rate of CFS grants indicates that they're not being treated differently than any other kind of grant that's coming in. That same concern about not having the right reviewer is one you hear in any of the IRGs. I think that Dr. Kitt will try to work with you. Every grant is given to three people to review. They fight it out in those meetings. From the

ones that I've observed personally or listened to on the telephone, they are extremely fair. It's a very fair process.

Dr. Hartz: I accept that they're fair. I don't think there's an inherent bias. But what I do think exists is there are some inherent difficulties with reviewing grants for CFS research. I'm not sure why the success rates are the same but I think the diversity of expertise that's required by reviewers of CFS grants is not the same as in other areas. I'm not sure that that problem has been addressed.

Dr. Hanna: Let's hope that the changes being made at CSR will lead to change and some innovation.

Dr. Jason: The reality is, if 15 percent of the members of this review group over the last two years have ever published an article in this area, and they're on a topic area that Dr. Kitt said that the CFS will go to, I just can't imagine that a person who has never published in this area can fairly review a proposal. I think 15 percent is an abysmal number and smacks of bias.

There was a time at NIH where there was money available for Center grants. That has changed.

Dr. Hanna: That was not allocated money. The National Institute of Allergy and Infectious Diseases decided that they would put out an RFA for Centers and they did. When those Centers finished—when it was time to re-compete—they chose not to do that on the basis of their own scientific reasons. The money was not allocated, it was a decision, just as we made the decision to put out the RFA on the neuroimmune mechanisms.

Dr. Friedman: I was a bit concerned this morning by what Dr. Kitt said. I have been through the peer review process and I know what it's like to be on the receiving end. In her reorganization I did not see any repair or consideration of the problem and that is, if you submit a grant and it is peer reviewed and declined for whatever reason and the investigator gets back the comments and then the investigator resubmits rebutting or correcting the perceived errors in the original application, that may then go to essentially a different study section or different reviewer or different set of reviewers who then find different problems that were not perceived in the first review. That grant gets rejected a second time. This goes on for a third and fourth time.

This completely frustrates the grant proposer. I would have liked to have seen a mechanism whereby all the criticisms of a proposal are laid out in the initial review and if there is a satisfactory addressing of all those criticisms, the grant would then at least be scored in a fundable range as opposed to having the investigator spend two or three months revising a grant just to have new "errors" appear in his grant application.

Dr. Hanna: I don't think she finished her presentation. She said that the changes would be announced, so I would recommend that you keep your eyes posted on the main NIH home page. All of those revisions will be up there. I have participated in some of these meetings and all of these criticisms have been brought up. They have to be addressed for everybody,

not just CFS, and they are making a good faith effort to do so. And Dr. Kitt is willing to work with this committee to specifically address CFS.

Dr. Jason: The problem that Ken brought up is unique in some ways to a special emphasis panel. A SEP is composed of potentially all new members for each of the three rounds, whereas a standing committee has that continuity that Ken is talking about where a member has several years of a term. The SRO has to be extremely sensitive to this issue in terms of assigning reviewers to the proposal. If that doesn't occur carefully, the field is at a disadvantage.

[Dr. Oleske called a break for lunch.]

Committee/Subcommittee Discussion

Dr. Parekh announced that:

- The process for CFSAC charter renewal would begin at the conclusion of the meeting and continue throughout the spring and summer. He assured CFSAC members that his office will keep them updated.

- The CFSAC website (www.hhs.gov/advcomcfs) has been upgraded to comply with Section 508 of the Americans with Disabilities Act and also reconfigured to make it more user-friendly. He invited committee members to make website suggestions.

Ms. Healy requested that a distinction be made on the CFSAC website between draft and approved meeting minutes. **Dr. Parekh** said he would make sure that minutes would be marked "Draft" until formally approved.

Concept Paper Leading to Surgeon General's Workshop

CFSAC members hammered out a draft recommendation to the HHS Secretary designed to eventually lead to a report on CFS from the Office of the Surgeon General as discussed at the morning session. The first step on that road was determined to be a recommendation to HHS Secretary Leavitt asking him to request that relevant agencies collaborate on a CFS concept paper that would lead to an OSG-sponsored workshop on CFS.

The concept paper would include data generated by CDC and NIH based on the state of the science. **Dr. Hanna** noted that the last State of the Science Consensus Conference on CFS was held by NIH in 2001. **Dr. Jason** questioned whether the HHS Secretary would have sufficient motivation to follow CFSAC's recommendation without documentation showing why it is important. **Dr. Oleske** wondered whether CFSAC could play a role in assuring the accuracy of the information that the SG receives.

Dr. Parekh suggested that CFSAC could emphasize to the Secretary the importance of its recommendation by drafting a short, powerful statement about the potential impact of a CFS workshop. The statement could provide examples of how past workshops significantly changed a field, such as HIV/AIDS. Dr. Parekh reminded the committee that many unknowns exist in the lengthy and uncertain process of working towards an SG-hosted workshop: whether or how the Secretary acts, how the agencies will receive the Secretary's request, how long it will take to develop a concept paper, and how a new post-election SG will react to taking on CFS as opposed to any other disease. Dr. Parekh added, however, that the end result holds a lot of promise as well.

Mr. Newfield suggested that before crafting a concept paper recommendation, CFSAC address the more time sensitive opportunity to influence the CDC's upcoming external review process. Dr. Parekh brought up another time sensitive opportunity—HRSA's offer to consider disseminating a letter on CFS to its grantees.

Before moving on to the more immediate opportunities, CFSAC unanimously passed the following draft recommendation, worded to include all HHS agencies with input on CFSAC issues. Members gave Dr. Parekh editorial privileges to fine tune the wording on this and all subsequent recommendations. This and other draft recommendations are listed together at the end of the minutes:

Draft Recommendation #1

CFSAC recommends to the Secretary of Health & Human Services to request HHS operating divisions to produce a concept paper on CFS to be considered by the Office of the Surgeon General for development of a future Surgeon General's workshop.

Preamble to be written by subcommittee chairs within 30 days.

CFSAC members suggested material to be considered for inclusion in the preamble:

- The economic and other impacts of CFS as presented in public testimony of CFS patients at CFSAC meetings.
- A possible statement of the purpose of the workshop—quality interventions, impacts, disparities in care, need for training, and need for research.
- Wording from the preamble of the previous CFSAC recommendation requesting a letter from the SG. This document appears at the end of the meeting minutes.
- Any ideas gleaned from going to the SG's website to determine what kinds of information the office is looking for.

The preamble will be distributed by email for review to all voting and *ex officio* members.

CDC External Peer Review

Dr. Jason suggested that the education of the next generation of health professionals to treat CFS patients is one of the most important issues before CFSAC. He said that the CDC's

program for training professionals needs to be closely examined, especially in light of the fact that the CFIDS Association is no longer contracted to work with the CDC. What is going on in the program and what is its future direction?

Dr. Oleske emphasized the importance of having proper representation on the review panel of providers from the CDC community. **Mr. Newfield** suggested that the CDC was also giving CFSAC the opportunity to suggest what the review panel would evaluate as well as who is going to participate. Sarah Wiley said that CFSAC is being asked to give guidance on how broad the peer review should be. For example, CDC is debating whether to limit the review to the research program or include the public awareness campaign. She also asked CFSAC to consider what—if not all—aspects of the research program should be reviewed.

Dr. Friedman put in a plea for the continuation of live presentations for educating healthcare providers. He said that it is a viable mechanism. **Dr. Oleske** suggested that research and education not be split into different areas of the CDC CFS program as they are now. **Ms. Wiley** said that the peer review is unlikely to address that organizational issue, but could examine both pieces of the program. She advised CFSAC to weigh in on how broad the scope of the peer review should be as opposed to providing specific issues to be addressed.

Ms. Artman said that the peer review should be as broad as the CDC can possibly afford in order to flesh out where shortfalls are and what's going right. A narrow review may miss something important. **Ms. Wiley** said that a review of all program aspects is probably not possible and advised that if CFSAC recommends a broad review, it should prioritize the areas to be covered. Committee members proceeded to discuss the scope of the review and recommendations of people to serve on the external review panel.

Dr. Oleske said that he favors the peer review process looking at combining the separate educational and research pieces. **Ms. Healy** noted that provider education is in the same part of CDC as research and that it is the public education program that resides in a different area of the agency. Dr. Oleske reiterated that he objects to the education processes for a disease being conducted in two separate parts of the agency. Ms. Wiley said that the Center for Health Marketing, which handles public awareness, works closely with the Communications staff in Dr. Reeves's group.

CFSAC members discussed what other areas—both broad and specific—to prioritize in their recommendation including:

- Etiology
  - Genetics
- Progress towards finding a biomarker, including ensuring that the large amount of data collected by CDC is being maximally used and that CDC has the resources to properly analyze the data.
- Provider education
- Treatments
  - Medications

- Assuring that the CDC is not insular and has leadership with a broad, unbiased approach to the disease rather that a single direction of thinking.
  - How CDC relates to the research community.
  - How CDC prioritizes its activities.

Before crafting a recommendation on the content of the CDC external peer review, CFSAC members wrote their recommendation on who they want to serve on the review. Members made a point of selecting female, clinician, and international nominees. The following recommendation passed with three abstentions from nominees who were recused from voting:

Draft Recommendation #2

CFSAC recommends to the Secretary of Health & Human Services that CDC consider the following specific individuals for its external peer review process of the CDC CFS research program - Drs. Christopher Snell, Anthony Komaroff, David Bell, Kenneth Friedman, James Oleske, Lucinda Bateman, Elke van Hoof and Birgitta Evengard.

CFSAC members then resumed discussing recommendations for what the peer review should actually cover. The following ideas emerged:

- The CDC has a unique population for which it already has a database. CFSAC should recommend that the review focus explicitly on the two most important areas for moving the field forward—establishing etiology and establishing biomarkers.

- FY 2007 budget material provided by CDC to CFSAC names the five funded areas of the scientific research program. These categories could help CFSAC ponder which areas the CDC should be emphasizing:

  1. Surveillance and epidemiology - $600,000
  2. Clinical assessment and evaluation (Emory inpatient study) - $1.2 million
  3. Objective diagnosis and pathophysiology, laboratory studies, meetings, workshops, computational models - $2.1 million
  4. Treatment and intervention (meetings and consultations) - $121,000
  5. Provider education - $300,000

  Ms. Wiley noted that the budget information was put together in response to a question and does not represent official CDC program categories.

- Should a peer review tell the CDC what it should be doing and what its priorities should be or merely assess how well the agency is meeting the priorities it sets for itself?

- What do CFSAC members want to know about CDC activities in the areas in which the agency is involved? What areas do CFSAC members want the external review

committee look at and report on? Members offered suggestions, some of which were a continuation of the discussion above:

- The quality of data that CDC is collecting on epidemiology.
- The search for a causal agent.
- Gene expression studies and research on other genetic topics.
- How the CDC sets research priorities, which would reveal whether the agency is making optimum use of their resources.
- How well CDC researchers relate to other research groups in a collaborative way.
- What is occurring in provider education, what has been accomplished, what is the vision for the future, and what resources are the CDC putting into it?

CFSAC members discussed what form their recommendations for the CDC external review panel should take. Some favored one broad recommendation encompassing all of the issues about which CFSAC is concerned. In the end, members decided to split topics of concern into several recommendations. The following peer review recommendation passed unanimously:

Draft Recommendation #3

CFSAC recommends to the Secretary of Health & Human Services that CDC's external peer review process focus on the program's progress on provider education, the search for specific diagnostic biomarkers, and the identification of CFS' etiology.

CFSAC members next crafted a recommendation that the CDC peer review panel examine the extent to which the agency's research agenda is personality-driven rather than collaborative and how the agency establishes research priorities. Dr. Hanna pointed out that this and other topics were also discussed in the CDC blue ribbon committee report that Dr. Miller would be providing to CFSAC members. She suggested that the report might give members some baseline information as the peer review moves forward.

The following recommendations passed unanimously:

Draft Recommendation #4

CFSAC recommends to the Secretary of Health & Human Services that CDC's external peer review process evaluate CDC's use of expertise outside the agency.

Draft Recommendation #5

CFSAC recommends to the Secretary of Health & Human Services that CDC's external peer review process evaluate CDC's establishment of research priorities.

CFSAC members then turned their attention to taking advantage of HRSA's offer to distribute CDC toolkits and other provider information through the AHEC network. The committee unanimously passed the following recommendation:

Draft Recommendation #6

CFSAC recommends to the Secretary of Health & Human Services that the Administrator of HRSA communicates with each Area Health Education Center regarding the critical need for provider education of CFS.

HRSA has the potential to disseminate information on CFS to a wide range of providers, communities, and educational institutions. HRSA should inform these groups that persons with CFS represent an underserved population and that there is a dramatic need for healthcare practitioners who can provide medical services to CFS patients. HRSA should further inform these groups that the CDC offers a web based CME program on CFS at www.cdc.gov/cfs; and encourages AHEC providers to participate in this CME program. Additionally, HRSA should alert AHECs of the availability of a CDC's CFS provider toolkit.

Adjournment

CFSAC May 5-6, 2008

Draft Recommendations:

CFSAC recommends to the Secretary of Health & Human Services to request HHS operating divisions to produce a concept paper on CFS to be considered by the Office of the Surgeon General for development of a future Surgeon General's workshop.

Preamble to be written by subcommittee chairs within 30 days.

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CFSAC recommends to the Secretary of Health & Human Services that CDC's external peer review process evaluate CDC's use of expertise outside the agency.

CFSAC recommends to the Secretary of Health & Human Services that CDC's external peer review process evaluate CDC's establishment of research priorities.

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