CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE
Meeting

Monday, April 24, 2006
9:00 a.m. to 5:00 p.m.

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

Agenda

U.S. Department of Health and Human Services

9:00 a.m.	**Call to Order**	Dr. Anthony Komaroff, *Acting Chair CFSAC*
	Opening Remarks	
	Roll Call	Dr. John Eckert *Acting Executive Secretary*
9:30 a.m.	**CFSAC Community/Organizational Updates**	Ms. Patricia Fero, *Executive Director* *Wisconsin CFS Association*
10:30 a.m.	**Break**	
10:45 a.m.	**CFSAC Community/Organizational Updates (Cont.)**	Mr. Fredrik Carlson, *President* *Vermont CFIDS Association*
11:30 a.m.	**Public Comments**	
12:00 noon	**Lunch**	
	Updates from the Federal Sector	*Ex-Officio* Members, CFSAC

[**Please note:** For clarity's sake, all Federal sector presentations are grouped together in this report even though several occurred later in the meeting.]

2:30 p.m.	**Break**	
3:00 p.m.	**Committee Business/Discussion**	
4:45 p.m.	**Closing Remarks**	Dr. Anthony Komaroff
5:00 p.m.	**Adjournment**	

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Members in Attendance

CFS Advisory Committee Members

Chair
Dr. Nahid Mohagheghpour

Voting Members *Present*
Rebecca Artman
Dr. Lucinda Bateman
Dr. Kenneth Friedman
Kristine Healy
Dr. Anthony Komaroff
Dr. Morris Papernik
Staci Stevens

Voting Members *Absent*
Jane Fitzpatrick
Dr. Nahid Mohagheghpour

Ex Officio Members *Present*

Centers for Disease Control and Prevention (CDC)

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

Health Resources and Services Administration (HRSA)

Dr. William A. Robinson
Director, Center for Quality

National Institutes of Health (NIH)

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

Social Security Administration (SSA)

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

Ex Officio Members *Absent*

Food and Drug Administration (FDA)

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

Social Security Administration (SSA)

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

Executive Secretary *(Acting)*

Dr. John Eckert, Office of Public Health and Science (OPHS)

Call to Order, Roll Call, Opening Remarks

Dr. Anthony Komaroff, Dr. John Eckert

Dr. Komaroff, serving as Acting Chair, called the meeting to order. Dr. John Eckert, OPHS, introduced himself and explained that he would be acting as Executive Secretary for the CFS Advisory Committee until the Assistant Secretary for Health appoints an Office of Public Health and Science staff member to permanently function in the position. Dr. Eckert then conducted roll call.

Dr. Friedman inquired about the status of the CFSAC subcommittees, including whether they will continue and whether Committee members need to review whom is serving on the subgroups. Dr. Komaroff stated that with many members rotating off the parent Committee, it might be wise to seek new subcommittee members. Who, in consideration of new Committee members, Dr. Komaroff suggested that further

discussion about subcommittees be delayed until later in the meeting so that new panel members could select their areas of interest.

The discussion moved to approval of the minutes for the September 2005 CFSAC meeting. Dr. Komaroff asked if there were any comments on the minutes. Dr. Friedman expressed his concern about a statement at the end of the minutes regarding the final motion made at the meeting. The statement read that the recommendation being made would be noted in the minutes but not forwarded to the HHS Secretary.

This statement initiated discussion about the procedure for handling recommendations made by the Committee. Dr. Komaroff asked if there were policies/procedures established for advisory committees to make recommendations to the Secretary. Dr. Eckert did not have knowledge of any procedures, but stated that he would check on that issue and provide advice to the Committee later in the meeting. A motion was made to delay approval of the September 2005 minutes until clarification of the policies/procedures could be provided. The motion was approved.

CFSAC Community/Organizational Updates

Patricia Fero, *Executive Director, Wisconsin Chronic Fatigue Syndrome Association*

Ms. Fero presented information that she received in response to Freedom of Information Act (FOIA) requests filed with the NIH CFS Trans Working Group and the Offices on Research for Women's Health and Extramural Research. The data she collected primarily covered NIH funding patterns when awarding grants for CFS-related projects. Ms. Fero requested and reviewed available data on NIH grant activity from 1999 to 2005. The data revealed that there was a line item in the NIH budget for CFS—approximately $5 to $6 million—but that NIH made very few grant awards for CFS-specific projects. Ms. Fero recalled that one reason given by NIH for the low number of CFS-specific awards was that not enough scientists appeared to be interested and the number of innovative grant proposals was few.

The most recent data collected by NIH indicates that the number of CFS-specific grant projects has increased; however, Ms. Fero pointed out that many of the grants are renewals and/or long-standing projects (i.e., CRG1, CRG5). There is also a discrepancy between the number of CFS-specific grants and the number of grant projects known to be active. In view of this discrepancy, Ms. Fero sees a need to conduct an evaluation and/or audit of the research funding process, specifically in relation to funds allocated for CFS research.

While the names of grant applicants cannot be disclosed, the number of applications received/reviewed can be obtained under FOIA. Based on information that Ms. Fero reviewed for FY 2005, it appears that NIH identified 55 grants as being for CFS research, but only 20 were for actual CFS-specific projects and only one new project

received funding. Ms. Fero discovered that some awards classified as funding for new projects were actually allocated to long-standing projects that had undergone revisions.

Ms. Fero questioned whether NIH still uses peer review groups to award grants for CFS research. She recalled that she raised this issue with the Committee in 2004 when she asked whether all CFS grant proposals had to be reviewed by a CFS special emphasis panel (SEP) and found through her own research that SEP review is not required. Ms. Fero presented a chart to reflect grant awards that had not been reviewed by a CFS SEP. She questioned the validity of the grant making process if the CFS scientific community is not given an opportunity to review proposals. She requested that the Committee review her information and make it publicly available, especially to CFS patients. Based upon her data covering 1999-2005, there appear to be more grants being funded by review panels that do not specialize in CFS than by the CFS SEP. Ms. Fero also noted that several grant projects approved for renewal did not include innovative approaches for addressing CFS. She expressed concern about the future of CFS-specific research if this pattern continues.

She also expressed concern about the lack of information about CFS on the websites of several pain and fatigue centers. She noted that there was no link on these sites to CFS organizations such as the Chronic Fatigue and Immune Dysfunction Syndrome (CFIDS) Association of America and the Wisconsin CFS Association. Ms. Fero viewed this lack of information as evidence that CFS is being discounted as a cause for an individual suffering from pain and fatigue. She concluded that there is scientific emphasis on pain and fatigue because those two symptoms occur broadly in many disorders.

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

Frederick Carlson, *President, Vermont Chronic Fatigue and Immune Dysfunction Association*

Mr. Carlson, who lives in Burlington, Vt., with his wife Barbara, chose not to share his personal story about CFS with the Committee, expressing hope that everyone in the room was aware that CFS is a real, debilitating, and long-term disease. He stated that he “had to assume that [the Committee] had heard or read the stories, and that [the Committee] is familiar with the morbidity studies that show that CFIDS patients experience a level of suffering that exceeds that of some heart attack victims, patients with rheumatoid arthritis, cancer, and even those in their final days of AIDS.” Mr. Carlson continued that he had to “assume that [the Committee] understands that the word fatigue does not even come close to explaining the degree of debility that goes on for weeks, months, years, and decades.” He did note that due to the personal discomforts that he has experienced as a sufferer of CFS, his appearance before the Committee is the most substantial activity he has taken on his own in 11 years.

Mr. Carlson has been president of the Vermont CFIDS Association for 10 years, and part of serving in his position has been volunteering to answer calls to a CFS 800 number. He told the Committee that CFIDS patients form support groups when conventional medicine fails, because there is nowhere else to turn but to each other. CFIDS patients are not particularly activists by nature, he explained, but no one wants to live with the limitations of such a disease. Mr. Carlson said that he receives several calls a day from patients who are seeking a doctor who can treat CFS because their primary care physician does not believe this condition to be real. Mr. Carlson said that he appears before the Committee to represent the CFS patients serviced by his organization. In doing his job, he repeatedly listens to people who feel they have nowhere to go, no one to turn to, and no one who understands. Mr. Carlson said that he tries to provide a sense of hope through the web page managed by the Vermont CFIDS Association.

Mr. Carlson maintained that many doctors first consider a psychiatric profile for CFS patients, which is encouraged by the CDC's awkward definition of the disease. CFIDS has been mostly treated as an illegitimate illness, he maintained, adding that because 70% of those diagnosed with CFIDS are women, it is being discarded as a "women's thing". Mr. Carlson declared that the manner in which many women are treated by the medical community is appalling.

The primary issue is finding a cure for this complex multisystemic disorder, he continued, but before this can be done, attention must be given to the repeated misunderstandings and misdiagnoses that have destroyed so many lives and families. When CFIDS is treated as a psychiatric disorder and the viral illness is ignored or denied, the patient worsens, he said. Mr. Carlson expressed concern about the negative impact of the name given to this health condition, including the fact that Vermont's traditional medical community has determined that CFIDS does not qualify for an insurance claim.

This stigma has made patients' search for a treating physician very difficult, he said. From the first psychiatric evaluation, reports of a CFS patient's condition are distorted, and the road to recovery becomes booby trapped by suspicion of secondary gain. In Mr. Carlson's view, the medical/pharmaceutical/insurance companies have overwhelming power over the health of CFS patients and are stifling and destroying all hopes they might have of receiving proper care and treatment. The power of these three industries has resulted in terribly ill people getting far worse, he said, and there is currently little hope that this will change.

In Vermont, plans are being made to pass legislation designed to educate primary care physicians about CFIDS using the consensus manual developed in New Jersey, according to Mr. Carlson. The 13 chapters in the consensus manual were developed so that physicians can appreciate the pathophysiology, differential diagnoses, and therapeutic opportunities, and the extensive bibliography will allow caregivers to further research CFIDS. Because of repeated misdiagnoses, educating primary care physicians is imperative, and the manual will give a legitimate starting point, according

to Mr. Carlson. Patients will be able to take the manual to their caregiver and by focusing on the chapters that are relevant to their condition, will experience a degree of empowerment that used to be unthinkable.

Committee Members Q&A

Ms. Artman: [To Dr. Eleanor Hanna] Is it possible for CDC and NIH to include a PDF file on their website that patients or physicians can download for basic information—perhaps a two page document that references organizations. Based upon personal experience with my doctor, we need something that we can use—like the New Jersey manual—as a patient base to educate physicians. Is that something that is realistic to ask for from CDC and NIH?

Dr. Hanna: We did put out a page of what to do when you visit your doctor that acknowledged a lot of these issues. The only non-government website that we can list is the IACFS, where people could look for other sources. Don't know if we could put up the New Jersey manual; will check on that.

Drs. Komaroff and Friedman commented on the manual, noting that Dr. Komaroff was one of the editors and Dr. Friedman served on the editorial committee. They reported that they have received requests from Japan for the manual to be reproduced in Japanese.

Dr. Reeves gave a brief presentation on CDC efforts to provide written material both electronically and in hard copy that provides resources to the CFS patient population. He said that such information is available on the CDC website.

Ms. Healy asked Mr. Carlson to provide details on the distribution plan for the New Jersey manual to allied health professionals, such as physician assistants, and he responded that the distribution plan does include these professionals.

Dr. Papernik recommended that the Committee look into designating or searching for areas in the country where physicians are known to have an interest in CFIDS (i.e., California, the Midwest, North Carolina, and Utah), and can become part of a web-based resource network where patients obtain information.

Dr. Komaroff posed a question to the Committee to obtain members' input: Without Centers of Excellence in place, how can CFS patients be identified and obtain referrals more efficiently? What can the Committee do to expand the number of Centers as well as the number of patients treated?

Dr. Reeves: I repeatedly hear the CFS community express concern over evaluation, treatment, and access to health care. Expanding their options is an important agenda item for the Committee. There is a problem with referral to CFS specialists. I think that family practice physicians should be trained to take care of CFS patients and as a whole, need to be able to deal with the disease.

There are two types of people with CFS--those who are being newly evaluated and those who clearly have CFS and need treatment. There is a great unhappiness with the psychiatric evaluation, but whether we like it or nor, 48% of those newly identified with a CFS-like illness have a readily treatable medical or psychiatric illness. These illnesses need to be identified and treated. A physician's goal is to work up a sick individual, identify a known cause for any ailments, and treat that cause when possible. I think that the psychiatric evaluation is terribly important.

We need to figure out how we can create Centers that provide care as well as conduct research. Clinical research is not always revered because it is not conducted with test tubes in the laboratory, but a lot of good clinical research can be done along side the basic research looking for the pathophysiology. The AIDS program links together treatment groups and research. Because the death rate for chronic fatigue is not as dramatic, I think that we have not really put in the effort to provide treatment and care for patients. There is a lot of good information out there, but there has not been the interest among and development of physicians to treat CFS as there has been with AIDS.

Mr. Carlson: The interest is not there because CFIDS does not bring a patient certain death like AIDS, nor is it sexually transmittable. There is no media sparkle. People suffer tremendously from it, however, and I think they deserve to have the same type of effort brought to bear that we have made for other diseases, and this includes training medical students.

Right now, there is a movement going on in medical schools called humanism. You wouldn't think we would need to have a rediscovery of humanism in medicine, but in fact, that is what is going on, because medicine got away from understanding the concept of humanism as we take care of patients. That is being taught now at medical schools. This movement in medical schools provides an ideal opportunity to raise consciousness about diseases like chronic fatigue syndrome. If we could link CFIDS to this educational humanism movement, I think we can then train the doctors in the future.

But to move it quicker than that – because that is going to take several years – we need to conduct treatment trials that link ordinarily disparate groups. The Health Resources and Services Administration would address the clinical care center component and NIH would address the research center component. That's asking people who don't usually work well together to work together, but that is what has to be done.

Public Comments

Fran Hissler: I am very interested in finding the best way to locate all the [CFS] studies going out all over the country. It would be nice to have one central location where all studies are accessible. Is there any research being done in the area of intimacy—specifically how CFS affects the reproduction area and genital function?

There is a listing of clinical trials that the NIH and other sites maintain, but there are relatively few clinical trials in CFS. Most of the research that is funded is enrolling the patients to study the pathophysiology of the illness. And I am not aware that there is a listing of such trials. However, there is uncertainty about a registry of the clinical trials being available.

Dr. Hanna: When the new studies are funded, I plan to put them on the NIH website so that people can seek out the researchers.

Dr. Mary Schweitzer explained the difference between myalgic encephalomyelitis (ME) and CFS. She said that ME is a recognized disease with a 30-year history in the United Kingdom. A diagnosis of ME is based on positive identification of a set of symptoms. In contrast, she said, a diagnosis of CFS is one of exclusion. The diagnosis of ME focuses on the central nervous system—a medical concept. A diagnosis of CFS focuses on fatigue, a term that is very difficult to nail down for the purposes of formal medicine. The U.S. insurance industry uses the World Health Organization's International Disease Classification Codes to classify diseases. In ICD 9DM, ME was classified under neurology at 323.9. In 1998, the U.S. removed that classification and no longer recognizes the diagnosis of ME.

[Dr. Komaroff called a lunch break.]

Updates from the Federal Sector

Dr. Komaroff declared that the main Committee business is addressing the status of various recommendations that the group has made in the past. Because many of these recommendations affect the agencies that have Committee representation, Dr. Komaroff suggested that these reps provide an update on how their agencies have responded to CFSAC. He suggested that these updates be followed with a broad discussion on the status of the recommendations.

The CDC Wichita Study

Dr. Reeves: The CDC is conducting a study in Wichita that received press coverage and has been mentioned at previous Committee meetings before it was launched. The study is at the center of many CDC CFS efforts. I want to begin with a discussion of the project, then discuss CDC's current research programs and the control strategy that the agency has developed.

The Wichita study objectives address concerns expressed in CFSAC recommendations: There is no known cause and biologic marker to diagnose CFS, only limited knowledge of its pathophysiology. Research efforts must therefore apply an integrated approach to

addressing CFS's characteristic disregulation of highly integrated bodily systems. Forming multidisciplinary research teams would provide a platform to conduct well-controlled, methodologically sound studies to clarify the pathophysiology of this syndrome.

We randomly sampled 34,000 households in Wichita with 56,000 adult residents, which is a quarter of the population. Between 1997 and 2000, we followed 7000 people selected by this random sampling process through telephone surveys. About half had CFS or a CFS-like illness, the other half were normal and non-fatigued. This was a longitudinal study over two years.

We conducted two-day medical evaluations of patients who had visited the Wichita clinic and could have possibly had CFS. The purpose of the evaluations was to rule out other illnesses. Results:

- 70 individuals had CFS, 58 agreed to participate.
- 128 people were classified as ISF—insufficient symptoms or fatigue—which means people with medically and psychiatrically unexplained fatiguing illness that do not meet the CFS criteria.
- 30 people had CFS accompanied by melancholic, psychotic depression, and 27 of these agreed to participate as a comparison group.
- Another group of about 32 had ISC accompanied by melancholic depression, and 28 of these participated in the study.

We randomly selected an equal number of normal, non-fatigued people and CFS sufferers from those who had participated in all four years in the telephone surveys. We matched well individuals to CFS sufferers in terms of sex, race, age, and body mass index.

The purposes of the study were to characterize the participants' physiologic and mental status, determine if we could stratify cases/identify risk factors, and identify biologic markers. We hypothesized that people with CFS would have measurable neuro-cognitive deficits. Problems with memory and concentration are important. We hypothesized that CFS sufferers would have measurable sleep pathology, different hypothalamic pituitary adrenal access function, different genetic profiles, and different gene expression profiles. We evaluated each participant carefully to make sure that nothing else was going on.

Medical Outcome Survey and the MFI

We classified illness based on the Medical Outcome Survey Short Form 36, which measures eight dimensions of impairment, and the Multi-Dimensional Fatigue Inventory (MFI), which yields standardized measures for five dimensions of fatigue. We developed a symptom inventory that was published in July 2005 in *Biomed Central*. The article has been accessed 7000 times.

Our study looked at the 1994 case definition of CFS. The problem with this definition is that it does not incorporate standard measurements that would assure consistency among studies. The CDC is using and recommending the measuring of impairment.

Dr. Reeves also emphasized that it isn't the fatigue that causes substantial reduction in activities, it's the whole illness. Many people have more problems with pain, memory, or concentration than they do with fatigue. We took four of the eight Medical Outcome scales that we thought best reflected this, and if one was below the population 25th percentile, we believed that the individual had sufficient impairment to have CFS.

With respect to fatigue, we took two of the five scales of the MFI. If a measurement rose above the 25th percentile, we believed that the individual had sufficient fatigue. And then we used the symptom inventory—a CFS individual had to have at least four symptoms in addition to fatigue, and to have a score above the 10th percentile of the nonfatigued group. We measured the cognitive function of participants with the Cantab computerized program; evaluated them in a sleep lab; measured autonomic nervous system function, endocrine, menoralic corticoids, gonadol hormones, growth hormones, and inflammatory cytokines; checked for co-morbid psychiatric conditions; and measured genetic polymorphisms, gene expression profiles, and proteins.

Cantab and Sleep Studies

Cantab measures attention, visual memory, working memory, and planning. People with CFS in our study had absolutely no impairment in cognitive function in spite of the fact that 88% of them complained of these problems. However, CFS was associated with measurable mental fatigueability, specifically in attention and memory. The people could function at the same cognitive level, but they had to work harder to do it. These results have recently been published in *Neuropsychopharmacology*.

We also did overnight sleep studies measuring 22 brain leads. We did not find sleep abnormalities associated with CFS—cycle disturbances, circadian rhythm disturbances, etc. However, most of the people scored badly on the Epworth. They reported excessive sleepiness, again a disconnect between what's being reported and what is measured. CFS was associated with a faster resting heart rate and significantly less heart rate variability, indications of sympathetic nervous system dysfunction. A manuscript detailing these results is in process.

Early Life Stress

We looked at early life stress and psychopathology. We used the short form of the Childhood Trauma Questionnaire. We also looked at the self-rating depression scale as a co-morbid condition. We looked at state trade anxiety and the Davis and Post Traumatic Stress scale. A manuscript detailing these results is also in process, but I can tell you that CFS is significantly associated with higher scores in each of the five trauma types, and the mean scores in each type are in the moderate range for those with CFS.

We also looked in a simple fashion at what I'm going to call SNPs—single nucleotide polymorphisms. There is a significant association with corticoid receptors, serotonin receptors, and adrenal hormones.

The study produced various associations, but none of them account for all of CFS. It is a complex illness. There are alternations in the whole body's way of reacting to things. CFS is not so easily explained as the result of a single mutation or environmental factor.

The Challenge Competition

We formed four teams consisting of members from CDC, NIH, FDA, private companies, and universities. Each team had a physician or psychiatrist, a person with biostatistics expertise, and someone interested in computational biology. Each team had six months do to evaluation of data sets. We wanted them to identify biologically and clinically meaningful information relevant to classification, diagnosis, and treatment of CFS.

Team one ["The Thyroxins"]: Examined the concept of allostatic load—cumulative wear and tear on the body due to its response to stressors of living. People with CFS were five times more likely to have a high allostatic load index adjusting for other variables. Using a supercomputer, the team also looked at SNPs that might predict CFS against a non-fatigue state. Researchers had 76% accuracy doing so, and found that three genes predict the outcome.

Team two ["The Blobs"]: Used partial least squares and principle components analysis to ask the question, "Can I see differences within this whole population?" The team found three classes of fatigue. Genetic difference distinguished the classes. Class 1 was associated with the genes for POMC and NR3C1. Class 2 was associated with polymorphisms in the genes for monoamine oxidase A and B tryptophane hydroxylaze, which are both involved with serotonin. Class 3 was associated with polymorphisms in other genes. The team then went on to look at gene expression profiles using a computer algorithm. Researchers identified two classes that were essentially well and one class with severe melancholic depression by measuring signal transduction, synaptic transmission, protein catabolism, and hedgehog signaling. Expression levels of two genes differentiated the fatigue classes.

Team three ["The A Team"]: Studied only female subjects using projection to latent structure, a complex mathematical computer algorithm for distinguishing things that you don't know are there. The team found that 17 clinical variables and 39 gene expression variables described this study population. Eleven of those variables related to heart rate variability and blood pressure. CFS gene variables are distinct, but there is some overlap. The team reasoned that if fatigue is what underlies CFS, let's look at the MFI, which measures the dimensions of fatigue, and quantitative trait analysis to correlate gene expression levels with the MFI scores. The team found that of the 20,000 genes measured, 873 (4%) were associated with MFI scores. The pathways were

metabolism, cell proliferation, apoptosis, and signal transduction. The five arms of CFS are activity reduction, physical fatigue, motivation reduction, mental fatigue, and general fatigue. A Team results correlate almost 100% with the mental fatigue seen in earlier cognitive functioning tests.

Team four [C3T3]: Used hierarchical cluster analysis to look at genes associated with fatigue, and created what was called a "heat map" using a computer program. This analysis highlighted the same group of genes as identified before. The results were published in *Pharmacogenomics*.

The four teams produced a total of 14 manuscripts. Duke researchers functioning as referees at the meeting asked that the data set be made available to them for an annual competition in June. The data set is also being used by New York University for its bioinformatics program.

The executive summary of the competition: Four independent teams used unusual methods. We are now trying to bring all of the approaches together to replicate in the current Georgia study. One common theme in the study results is abnormalities in various stressors, or allostatic load, and the systems that respond to stress: the HPA axis, limbic system, and brain stem (physical stressors). All stressors affect the hypothalamus and activate a corticotrophin-releasing hormone, which then affects the pituitary gland, adrenal glands, immune system, neuroendocrine system, sympathetic nervous system, and musculoskeletal system. That is the model that we are currently going on.

Committee Q&A

Q: Wouldn't you expect large numbers of children who were Katrina victims to exhibit CFS in the future?

Dr. Reeves: Much of the interest at CDC now is exactly what you are saying. My bet is that there is going to be a huge amount of that in the wake of Katrina. Gulf War illness was quite similar.

Dr. Komaroff: You seem to be presenting evidence for two different things. One is a greater burden of stressors across a lifetime and the second is a genetically-determined alteration in the response to stress—that is, regardless of how much stress you face in life, you respond to stress in a physiologically different way. Is that right?

Dr. Reeves: That is correct. The brain is a plastic organ. The brain reacts and actually changes its physiologic structure based on stresses. This is one of the reasons that this is complex.

Q: Is the CDCSI available and is the MFI report proprietary?

Dr. Reeves: Forms are readily available and algorithms can be loaded into a Palm Pilot.

CDC and CFS Public Health Research

We are studying CFS and chronic unwellness in Georgia in metropolitan Atlanta, urban Macon, and in rural populations. Atlanta is the fastest growing metro area in the country and the largest in the Southeast. In Atlanta, we randomly screened 3000 households that contained 4400 residents. In Macon, we randomly screened 4400 households containing 4200 residents. We also screened 5000 households in surrounding rural populations. We screened by phone through one household respondent. We asked, "Is there anyone who you have noticed has been fatigued over the last month?" We also asked about unrefreshing sleep, problems with memory or concentration, and pain. A "No" answer to all of these questions meant that a person is considered well. Yes to any of those questions meant that the person is considered unwell.

Screening results showed that 56% of the populations were well; 44% were identified by the household respondent to have one of the four "unwell" conditions. Of those, 26% were unwell without fatigue and 18% were unwell accompanied by fatigue. We attempted to do substantial phone interviews with those who were unwell with fatigue: 80% agreed to do so. We also randomly selected a sample of those who were unwell but did not have fatigue as well as a similar number identified as well.

We classified those who met the case definition based on information gathered during the phone interview as having a CFS-like illness and invited them for a one-day clinical evaluation. Of the 469 who did not report an exclusionary condition, 177 or 38% refused to come to clinic and 292 came in for an evaluation. We also examined a similar number of "unwell without fatigue" and "well" participants matched to the CFS participants based on sex, race, and age. These clinical evaluations were similar to the Wichita two-day in-hospital evaluation, but included gene expression studies that had not been performed in Wichita. By June we will have complete results based on stress and allostatic load.

We are beginning a physicians' registry to be piloted in Macon.

Committee Q&A

Q: Ages of participants?

Dr. Reeves: 12-60.

Q: What were the exclusionary factors?

Dr. Reeves: The exclusionary diagnoses are those recommended in the case definition. In the clinic, about 48% of the people who complain of CFS-like illness on the phone have a medical or psychiatric diagnosis. Medical exclusions are thyroid disease, hypertension, diabetes. Psychiatric exclusions are substance abuse and alcoholism, melancholic depression, bipolar disorder, various psychoses, and anorexia/bulimia.

Q: Was obesity exclusionary?

Dr. Reeves: Yes, but I don't remember the percentage. A body mass index over 40 was exclusionary. Obesity is a problem in chronic fatigue syndrome, probably because of deconditioning.

Control of an illness consists of decreasing the morbidity of the population—which is a function of the prevalence and duration of the illness. A million Americans have been identified with CFS and have been ill for an average of at least six years. The average family in which someone has CFS foregoes $20,000 a year in annual earnings and wages. CFS costs the U.S. $9 billion a year.

How do we control these factors? You have to find the people with CFS and get them to intervention, take care of their illness. They have to have access to healthcare. In Georgia, we'll know the baseline prevalence, duration of illness, impairment, and economic impact. We can look for measurable changes in these over time. In Georgia we will be able to target those who don't have access to healthcare. We can also measure and target those who don't make use of healthcare. We are on the way to a reproducible case definition of CFS that will give the same answers anywhere it's used.

None of this research will be helpful unless healthcare providers know what to do. We have a provider education program that the CFIDS Association of America is responsible for. The initial program started with HRSA and it is now going into the medical schools. We also have a national public awareness program with CFIDS.

Lindsey Polonek, *CDC National Center for Health Marketing*

I will briefly discuss the CDC CFS public awareness program, for which I'm the project officer and which we conduct in conjunction with the CFIDS Association of America. The campaign is still in the planning phase and is scheduled to launch on June 7 at the National Press Club.

Target audiences: women between the ages of 40 and 60 and health care professionals including nurse practitioners, physicians' assistants, and primary care providers.

Objectives by audience segment: Women—change attitudes beliefs and social norms to reflect that CFS is diagnosable and treatable. Increase knowledge of symptoms and encourage the seeking of treatment from formal health care professionals. Women are often the main channel for health information within their families. Campaign website: www.cdc.gov/cfs. Using a "push approach" to push women and those within their family unit to the website to find downloadable materials to take to healthcare professionals.

Healthcare professionals—We also want to change attitudes and behaviors to reflect

that CFS is diagnosable and treatable. We want to increase awareness of credible CFS info (website).

Series of interventions developed: Traveling photo exhibit, "The Faces of CFS", which will go to medical meetings, high-traffic public venues, and the CDC; TV and radio public service announcements; print ads in *Better Homes and Gardens* and *Ladies' Home Journal* in beginning in July 2006 issues to run for five and four months respectively; variety of materials on the website. We have a small batch of print materials, but the main drive is to the website. Materials there include patient cards and assessment tools, a toolkit for professionals, a resource guide, and a series of fact sheets for both the public and professionals.

Dr. Reeves: This campaign is the primary responsibility of the new CDC Health Marketing Center, which is staffed with marketing professionals.

Committee Q&A

Dr. Oleske: [Offered CDC congratulations on its research and awareness campaign.] As an immunologist, I'm interested in the neuro/immunological/endocrine axis. Is this information available?

Dr. Reeves: *Neuropsychopharmacology* is out, but not all PDF versions of other articles are available for distribution. The exact measures that we did in the study are either published or in preparation.

Ms. Fero: Are you looking at increased funding within the CDC? How is it that you can do both Wichita and Georgia studies? Why are CDC and NIH making separate efforts? Why is there no more collaboration, which would provide a much better outlook for patients?

Dr. Hanna: Many of Dr. Reeves' methods and hypotheses were developed from NIH studies, which are doing the basic research in laboratories and through extramural funding, plus its human genome project. We can only fund the proposals that come in and we are sending out requests for proposals dealing with CFS.

Dr. Reeves: CDC has met with the NIH Trans Working Group to discuss an international collaborative group.

Dr. Bateman: What is the funding outlook for CDC continuing this level of research and carrying it on and expanding it? What can this committee do to help?

Dr. Reeves: All of the agencies are having severe problems with funding. Our current funding has been cut 66% [for fiscal year (FY) 2007]. Basically, at the end of the second year of the program, the program will stop, or at least undergo major changes.

Dr. Oleske: Specific budget numbers?

Dr. Reeves: Funding has been $9-10 billion a year since 2000 and will be just slightly under $4 billion for ’07.

Dr. Oleske: To what extent is this slowing your momentum?

Dr. Reeves: The second round of the Atlanta study has been funded in ’06, and because it is under a contract, may continue into ’07. An in-patient general clinical (NIH) research center study at Emory University also has been funded in ‘06 under a contract that extends into ’07. When the current phase of these contracts expires, there is no more funding for large population studies.

Dr. Oleske: The studies with baseline data and periodic sampling are very important, hard to do. You’ve gotten so much of the data started, isn’t there a way of developing some sort of support for a long-term follow up to give us some answers that only a long-term follow up would do?

Dr. Reeves: As we become more aggressive, there are other centers at CDC interested in aspects of this—the injury center is very interested in the early childhood and economic aspects of this as well as suicidality. We try to spread the portfolio around. We’re also expanding the portfolio to include the military, but these studies are not the large kind of population studies. The leadership of CDC is on board with what we’re doing, but they must decide with the amounts that they have, where they are going to put that?

Ms. Stevens: Mr. Chairman, we made a motion to continue the funding for CDC at the same level or higher. What has happened to that motion?

Dr. Eckert: It is my understanding that Dr. Zucker received that recommendation from the person who was acting chair last year—John Jarmon. I do not know what the status is of that recommendation or the others that were made by the Committee. I have only caught up with one person who would know, and he told me that Dr. Zucker did not forward the motions or the recommendations to the Assistant Secretary or the Acting Assistant Secretary at the time, Dr. Piatto. Will check on status of this.

Dr. Oleske: Was quality of life studied?

Dr. Reeves: Wichita, no; Atlanta, yes. But we haven’t analyzed the Atlanta data yet.

Dr. Oleske: The reason CFS doesn’t get enough attention is that we fail to measure the tremendous negative impact on quality of life. I’m going to guess that it’s going to show that CFS victims have a much lower quality of life.

Dr. Reeves: Will be able to observe quality of life in urban area and more conservative rural locations—I suspect that there will be some differences.

Noted: A written report is available from the FDA, but a representative from that agency did not make a presentation as scheduled. The SSA also cancelled its scheduled appearance.

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

Report on the RFA – We had 29 applications that came in and were reviewed. There will probably be a 23% success rate on the applications, which will be awarded towards the end of May.

I will make material prepared for Congressional appropriations committees available to the CFSAC in May after the Senate hearing.

We're switching to an electronic filing for grants. There will be separate transition periods for RO1s and R21s, but the announcement of the switchover will be the same.

The shift in the method of percentiling, you've already heard about this morning. If we could get 29 applications for the RFA, then we could get close to 25 to come in on regular study sections, and then we could have our own study section. The way the study section is set up now is that it is a combined section that includes fibromyalgia, TMJ, and CFS. The reason that the percentiling can change is that the combined total of them all came to 25. So if we can get the numbers up coming in, then we can have our own study section.

[Dr. Hanna presented a printed out version of each of her office's main website pages. Asked group to log on to interact with the site and provide feedback. The site goes beyond usual NIH practice and includes patient-specific information.]

ORWH is now putting out a series of fact sheets. The first is going to be about CFS. Information is from the neuroimmune mechanisms meeting. The second fact sheet is going to be about pituitary disease. The one depression that is linked with pituitary disease is melancholic disorder.

ORWH is planning two future meetings – one on CFS throughout the lifespan, which encompasses children, and the other covering the doctor-patient relationship and how it factors into treating problem illnesses.

We will have to have a review of all CFS research at NIH to decide where we should move next in the CFS working group.

Committee Q&A

Ms Artman: Could you tell new members about the NIH working group?

Dr. Hanna: It is all on the website—it would take up too much time to present it fully today. The site has history, plus what's happening now.

Dr. Friedman: CFS is not defined as a woman's disease. I am concerned over a fact sheet coming out of the women's health office.

Dr. Hanna: The topic is what is NIH doing about CFS? It isn't going to be focusing on women. It's just that our office is doing this. CFS is the second most requested page on our website. The neuroimmune meeting proceedings is the most requested document.

Dr. Friedman: Are you going to do mortality data when examining CFS across the lifespan? As far as I know, there is no mortality data that would indicate whether or not people with CFS die prematurely or because of particular causes.

Dr. Hanna: We are interested in following the trajectory of CFS, the natural history or prognosis, in different age groups and how some younger people may grow out of it, etc.

Dr. Friedman: I would encourage you to consider trying to do it in older populations to determine mortality factors.

Ms. Stevens: How many proposals will it take for a separate CFS study section and how soon can that happen?

Dr. Hanna: I'm not sure. We must have 25 or more proposals and this momentum has to be sustained for a year and a half.

Dr. Friedman: What about making a different combination for study group review that includes Gulf War Syndrome?

Dr. Friedman: CFS is under diagnosed in minority populations, so it is difficult for them to be recognized and treated. It's counterintuitive that minority populations wouldn't have an increased risk of CFS due to more exposure to trauma in childhood. I would hope that NIH and CDC would try to figure out how to study that issue.

Dr. Hanna: We bring that up in our information.

Dr. Friedman: I just don't see many African-Americans in treatment programs.

Dr. Reeves: CFSAC has had extensive discussions about this in the past: the people who see physicians are white women, and they're generally educated upper middle class professional women with sudden onset of disease. CFS numbers were two times higher in the black population in Wichita and five times higher in the Hispanic Chicago population. It is at least as high in those populations overall. Socioeconomic status is even more important. A household that has less that $40,000 a year in annual income

is significantly higher.

Dr. Papernik: I worked with Lenny on the epidemiological studies. We had to identify the population group that we were going after and draw them in with phone surveys.

Dr. Komaroff: I am concerned that since the CFS RFA is complete, investigators may not know that NIH is still interested in CFS-related proposals. Should a communication be sent out to those who previously submitted proposals?

Dr. Hanna: I have already sent letters out to everyone who responded to the RFA. I will try to get the names of unsuccessful grantees over the years and write more letters. I will also post our interest in CFS on website.

Dr. Bateman: Seems like good timing to do that, with renewed interest in the CDC studies. There really is a feeling among some investigators that it's hopeless to try to submit a CFS proposal.

Dr. Reeves: With regards to the NIH interest in funding CFS research, I would point out that the pay line for CFS grants is a bit better than the average for grants on all topics. One of the concerns, though, that I hear from grant applicants is that when they revise an approved but unfunded grant to reflect the critique of the study section, a new study section reviews the grant and has completely different critiques. Is there a way of coordinating the review of resubmissions?

Dr. Hanna: We have been working on the review of repeat grants.

As for whether there will be another similar RFA, unfortunately none is planned. That is because there is no money for one. In fact, very few RFAs will be coming out of NIH for any research subject because of the tight budget. I could arrange for program officers or even grantees to appear before CFSAC to discuss research.

Dr. William A. Robinson, *Director, Center for Quality, HRSA*

We don't have any programs that are specifically designed to address chronic fatigue syndrome. The agency has an eclectic group of programs, from community and migrant health centers, which devote $2 billion to care for the underserved, to administering the Ryan White Care Act (funds for patients with HIV/AIDS for meds and comprehensive care), to administering maternal health block grants and the Healthy Start program.

We have had a series of programs that target the health professions in terms of training, but the Administration has zeroed all but programs for nurses. Most of the training for pediatrics, family practice, and minorities in medicine has been a victim of budget cuts.

Other HRSA programs include:

- Rural health care.
- A $500 million emergency preparedness program to ready hospitals to cope with a bioterror disaster.
- The nation's organ donation/transplantation program.
- Children's Hospital Graduate Education Program.

HRSA's Health Information Technology Office, which encompasses the Advancement of Telehealth, may interest the CFSAC because of the relative scarcity of CFS practitioners around the country. It may be that there is some alternative to scattered CFS practitioners if we take the expertise that we do have and somehow make that available using remote technology.

Even though we didn't have any dollars specifically appropriated for CFS, we did work through the CFIDS Association of America on a provider education program that eventually resulted in the collaboration between CDC and the CFIDS Association. Dr. Reeves was called in because we didn't have the resources to underwrite the cost of this.

We've been trying to work with the CFSAC education subcommittee, where we made some outreach to health professionals' training institutions by looking at curriculum and whether or not the schools might want to become partners to help reshape their curricula, although the Federal government has no power to dictate any aspect of curricula.

Nurses would be a good advocacy group to connect with—they are often viewed as more compassionate and they are tuned into patients. The Administration is going to continue to support them because we still have considerable shortages. I can take message back to the Division of Nursing if the Committee wants to work with it.

Dr. Friedman: I would encourage that kind of leadership, not only because nurses provide most of the hands-on care and have the time to care for patients that physicians don't have, but because nursing schools are often affiliated with medical schools.

Dr. Robinson: I'm not talking about directing resources, though; just facilitating a discussion.

Dr. Bateman: I have been offering continuing medical education conferences in Utah, and nurses have been some of our most enthusiastic participants and supporters.

Dr. Papernik: If we were to go to our respective medical schools to discuss including CFS somehow in the curriculum, would we be able to say that we have your blessing?

Dr. Robinson: It wouldn't get you anywhere to use my name—nobody knows who I am. The Committee has taken the step of contacting the Association of American Medical

Colleges with the thinking that we would go to the organization that represents the schools rather that doing it on an individual basis. The association was non-responsive. We asked them to share what was in their curricula associated with chronic fatigue syndrome, and that's where the stone wall came in. I think that if the association would not respond to the Committee, it's unlikely that you would get a different kind of a reaction on an individual basis.

Dr. Papernik: Our situation at Rush is that we have a student with chronic fatigue syndrome, so we know the implications for the ability to learn. By taking it one school at a time—the dean at Rush at least understands the illness a little bit better now and possibly would be more amenable to having that within the curriculum.

Dr. Reeves: CDC's provider education program that we're doing with the CFIDS Association has taught me that there are two kinds of providers: those in practice who need CMEs to keep their license and those in medical school. We have reached out to the five leading universities that teach family medicine and said that we want to come on an annual basis and give grand rounds. The school doesn't have to do anything—we give them free grand rounds with a pre- and post-round survey. It works very well, but we're giving them something for free. If you just ask them to put it in their curriculum, you'll get a "no" because that's hard work. The grand rounds are given by CDC and CFIDS staff.

Dr. Friedman: I agree with Dr. Reeves that getting it into the "curriculum" is not the way to go. Offering free grand round as a supplement to curriculum is accepted.

Ms. Stevens: Two years ago, we were asking the wrong questions (by mailing the letters) and we got no answers. Now we're offering grand rounds. If we continue the education subcommittee, we can revisit the issue and ask about lessons learned and implement them in the future.

Dr. Reeves: Also, nurses have grand rounds, PAs have grand rounds, and it's not just grand rounds—it's continuing education credits. We just need to have measurable outcomes in an evidenced-based approach.

Ms. Healy: Our job is to get the educators excited about whatever it is that you want included. CFS is a helpful one for teaching differential diagnosis, for example. Dr. Robinson, what results did you get in sending letters to community health centers about CFS? Is there a way to target community health centers for provider education?

Dr. Robinson: The letters were sent to centers to let them know, based on the recommendations of this panel, that we think it's important to serve those who walk in with CFS. We included in the letters info from the CFIDS Association. We did not make an effort to follow up at that time. Ms. Healy, have you had feedback on website, train the trainer programs, etc.?

Ms. Kim Mcleary: After letters and materials went out, we had a flurry of people logging

onto the self-study course on the website, but unless they specifically included in their demographic the information that they were working in a community health center, we would have no way of knowing. With the advent of the awareness campaign, we'll have some new materials that we can push out through those networks of clinicians. We have also enhanced our evaluation measures.

Through the awareness campaign, we do have a partnership element and have invited as primary partners the American Academy of Nurse Practitioners, the American Academy of Physicians Assistants, the American Academy of Family Practice and 40 other professional and health oriented organizations.

Dr. Robinson: A continuing question—what is the best way to share information? Printed material is fine, but you don't know if anybody sees it or what they do with it. We have to keep promoting the CDC and NIH websites as being the two definitive sources of information. What I'm going to try to do with our website is to have people refer to the existing sites where the expert information is.

I would like to convince grand round providers to videotape presentations. It would take "many, many, many years" to reach every medical school. Providing recorded grand rounds might be a good use of resources, both for those who can't get to grand rounds and for CDC, whose budget is being cut.

Dr. Friedman: Can one grand round presentation be applied to all cases?

Ms. Kim Mcleary: Right now, each presentation has been tailored the requests of the program. But as the requests increase, that's going to get harder to do. We've been trying to sort of "get it right" and figure out what the audiences really want.

Dr. Friedman: As an educator who provided both the CME and grand rounds courses, I wonder if the status of who can give the courses can be clarified and if we can train more people in various parts of the country to give the courses to be able to respond to the need.

Ms. Kim Mcleary: Because we're in the formative stages, they've wanted to have some quality control and we only have a few people doing the presentations. Hopefully they'll allow us to expand out to other individuals.

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

Committee Business/Discussion

Dr. Papernik: There seems to be no resolution of any of the recommendations that were put forth during the last meetings, and I'm not sure that it's a wise idea to continue

with new business until we get some answers to the resolutions that were put forward last time.

Dr. Friedman: I concur with Dr. Papernik. I think we need to have answers. Can we establish a time frame? Dr. Eckert, what is a reasonable time frame for motions that have been sitting around a year, possibly more?

Dr. Eckert: With respect to the 11 recommendations—they have been forwarded to the Secretary and there was at least one meeting if not more than one meeting with folks to discuss the recommendations, although I don't know who attended the meetings. We've gotten some reports on specific recommendations from the agencies themselves, which is where most of the recommendations actually lie. I can follow up on that, but to give specific answers, I can't give a timeframe right now. I will try to get answers by the next meeting.

Ms. Stevens: I'd like to suggest that you've had two years to respond to our recommendations, and we've received nothing in writing. It is very reasonable to ask for a 30-day window. We can't move forward until we have some answers in writing. I'm personally very dissatisfied.

Dr. Reeves: Committee should think seriously about which recommendations they're talking about. There are some made at the last meeting that have not been answered yet. The recommendations set forth on Aug. 23, which all of the agency people participated in—we are in fact doing many of those things and we're doing them because of the Committee (multidisciplinary research teams, complex research). We haven't had to have direction from the Secretary.

Dr. Komaroff: It seems to me that members of any advisory committee are owed a written response to written recommendations that they submit. I have been a member of federal advisory committees for 35 years and I have never seen an instance where remarks of a committee were not responded to for two years. I will recommend that this Committee request a response, and soon. We cannot demand an acceptance of all of our recommendations, but we can demand a response. Given that this Committee has Congressional oversight, I would think this is what Congress would want as well. We have the right to express our unhappiness to Congress and the Federal government.

Ms. Stevens: I suggest that recommendations go on the CFSAC website in the "Resolutions" section. This shows the public that the Committee is doing something useful and avoids miscommunication with patients.

Ms. Healy: It is discouraging to see such old information on the website. More dialogue on keeping it current would be useful to me as new member and to the public.

Dr. Robinson: Some of the things in the recommendations have to do with the '08 budget. The '07 budget has already been submitted, so it's too late to change that. But while internal discussions are going on, we should prioritize those things that deal with

dollars or ’08 issues. You cannot afford to wait until your next meeting to bring those up again.

Dr. Hanna: Advocates have tried to get Congress involved in getting recommendations acted upon.

Ms. McCleary: We’re only aware of two member of Congress who have gotten replies from the Secretary to their inquiries about the status of CFSAC recommendations. There seems to be a rather broad silence.

Dr. Papernick: Wouldn’t it be advisable for us to set a 30-day time limit on replies from the Secretary rather than wait until the next meeting so that we can stay within the appropriate time frame to influence appropriations?

Dr. Robinson: I can’t speak to a specific time limit, but I think that you’ve made it clear to the Executive Secretary that your expectation is that he follows up immediately following this meeting with the people who are in the hierarchy above him. Knowing that he is a man of stature, otherwise he wouldn’t be sitting there, he will be able to go ahead and pass that message on. What he cannot guarantee is how quickly the people above him will be able to move. If you didn’t get a response within a month, what would be your next move? I don’t know that you want to get into that kind of “you better answer within a month…” mentality. I think it’s clear that you want an answer soon. Rather than waiting until the next meeting, though, determine what next action you would want when your message is received.

Dr. Reeves: I would recommend that the Committee arrange its next meeting to include the Secretary or his staff to discuss the status of the recommendations. Perhaps even members of the legislative arm who are interested could attend the same meeting.

Dr. Komaroff: [Called for motions on the issue of a response from the HHS Secretary.]

Ms. Stevens: I would like to move that we invite the Secretary to our next meeting and that we schedule our meeting as soon as he can meet so that we move this along.

Dr. Komaroff: Could you add to that the expectation that he will have read and be able to respond to the recommendations that the Committee has already submitted?

Ms. Stevens: [Added the verbiage suggested above.]

Dr. Komaroff: That would include the recommendations forwarded in August 2004 as well as the recommendation last September about the CDC budget.

Ms. Stevens: Correct.

[The motion was seconded.]

Ms. Artman: As a new member, wanted to add more explicit discussion to Recommendation 4 of long-term follow up to studies like the ones in Wichita and Atlanta, including quality of life issues.

On Recommendation 7, I would take advantage of linking chronic fatigue in medical schools to whatever we can link it to (humanism in medicine, or whatever an individual school calls it). I think we can have some influence.

Recommendation 8: Should reflect the fact that a physician's inability to recognize and treat CFS should not result in the patient being denied medical care for the disease or the ability to see another practitioner.

Recommendation 10: Concerned over classifying it as a nervous system disease when it's so complicated. Multiple organ systems are involved—it's a neuroendocrine immunological disease, from what I've heard from the CDC. I would like to see a change in the environment in which mental illness is considered something which is considered important and less legitimate in its complications and negative impact on patients. I think we should as a group encourage embracing mental health as a legitimate group of diagnoses that can affect someone with a chronic illness.

I want to reemphasize Recommendation 5 to include older children and adolescents in studies; to not include them is an error. Children represent a stage of chronic fatigue in which we can uniquely observe the pathogenesis in a much cleaner patient group.

Dr. Bateman: As a clinician, I have a few comments. I'd like to caution all of us that as we take these study results to the clinical community and teach people about how to identify patients that we convey what the difference is between a research case definition (cleaner, fewer complications) and a clinical case definition (more complications, morbidity, mental health, etc.).

Ms. Healy: Recommendation 2 needs to be updated because the RFA has already happened.

Dr. Komaroff: We have two choices: call for a response to the two-year old recommendations or update them. I think it would be more efficient to take the former track.

Dr. Reeves: I would strongly recommend against recasting recommendations. Follow up on the ones that you have because they have been made and not responded to, but have been under consideration. If you start trying to rework them, you are constrained by the fact that the Committee has to do so in open session and by the fact that they will be new ones.

Dr. Komaroff: [Called the motion; the Committee approved the motion.] We had not taken action to comment on the minutes of the last meeting because of some unresolved issues about feedback. We've now dealt with that. There is still the open

question of the meaning of the very last sentence of the minutes from the last meeting. We could strike the sentence, then get an explanation of whether it was conveyed to the Secretary.

Dr. Friedman: Another item needs to be addressed on page 7, item number three, a discussion by Dr. Zucker by phone. He commented that some of the Committee's recommendations were outside of the HHS purview. The Committee should have an explanation from HHS for which of the recommendations are in fact outside of the Department's purview.

Dr. Komaroff: If we meet with the Secretary and he responds, I assume that will be part of his response, saying, "This is nothing that I can control."

Dr. Friedman: Under those circumstances, I would go ahead and approve those minutes. There are a lot of good things in those minutes.

Dr. Komaroff: Under those circumstances, I move that the minutes be approved as they are so that everyone can see what glaring errors and what problems this Committee has been up against. There are two factual errors that need to be corrected. On page 2, the very first page of the minutes, it refers to the recommendations to the Secretary of August 2005, but I believe that should be August 2004. On page 17, it identifies human herpes virus 6 as a virus that causes measles. It doesn't—rubeola causes measles. Herpes virus 6 causes roseola.

Dr. Robinson: On page 4, it states that I said that the Federal government does not offer CME credits. My agency in the Federal government—that's HRSA—doesn't, but CDC, the Veteran's Administration, DOD, lots of others have programs that do offer CME credits.

Dr. Komaroff: Should we just change the Federal government to HRSA?

Dr. Robinson: Correct.

A motion was made and seconded to approve the minutes as edited. The Committee passed the motion.

Dr. Komaroff: Next meeting date – we had talked among ourselves about the date roughly three months from now on July 31, but the alternative suggestion has been made to seek the ability of the Secretary to join us, which realistically would mean that the Secretary would determine the date. Should we set the date for the 31st? unless the Secretary can be here sooner? Dr. Eckert, will someone solicit our availability around the 31st?

Dr. Eckert: I will be sending a message out to everybody. I'll invite the Chair of the Committee to send an invitation through me to the Secretary. I will send a memo encouraging Secretary Leavitt and other HHS leaders to attend and participate actively

in the next meeting, which I will recommend be scheduled on or around July 31.

Dr. Komaroff: I will draft a letter. [Committee members decided that they did not need to approve the draft before it goes to the Secretary.].

Dr. Bateman: There are at least three people on our existing Committee rotating off in September. I think we're already understaffed, and I would just like to know what preparations there are for identifying new people or extending the commission of those who are already here until we can stabilize some of these ideas and suggestions.

Ms. Healy: I would first like to know when the last member for this round of appointees will be appointed. We have one member yet to be appointed. Can we attend to that first, then go to new members?

Dr. Eckert: There is one outstanding seat available and I understand that we do have some candidates who are currently being vetted through the ethics process. I would hope that we would have an appointment made relatively soon, hopefully within a month and preferably certainly before the next meeting.

Ms Healy: Could you make sure that Olga Nelson has gone through the process of renewing the charter for the Committee?

Dr. Eckert: I have made a note that the charter is up in September, and am going to be following up with Olga and others to make sure we get that charter renewal process going.

Ms. Healy: I think that it's really important for a committee of this nature with such important work to have some institutional history. To lose so many members at this time would be difficult for those of us who are new to get up to speed as quickly on our own. If we had some of the members who have been around for a good period of time, I really think it would be helpful, if that's something that can be arranged.

Dr. Eckert: I'm going to look into the FACA rules for the extension of current Committee members as well as the number of consecutive terms that a member can serve on a committee. The Committee lacks institutional history, including in my own position as Executive Secretary. This Committee has had four secretaries in five meetings, and that's not fair. If we don't have a permanent Executive Secretary by the next meeting, then I will be here to provide that continuity from one meeting to the next.

Dr. Bateman: As a new member, I'm not quite sure what the existing subcommittees are on this Committee.

Dr. Komaroff: So many people have rotated off that our subcommittees are decimated. I think that we have to decide as a group whether we want to put off until the next meeting—which will hopefully be with the Secretary—the question of reconstituting our subcommittees with new members, or focusing each of them on

specific issues that arise at that meeting. It's a fair amount of work, and with more fundamental issues about both the endurance and the impact of the Committee on the table, it may be hard for people to spend a lot of time on issues that are less substantive than that until there's a sense of where the Committee as a whole is going.

Dr. Bateman: I support that. I think that we have to stabilize the Committee as a general committee before branching off.

Ms. Healy: Agenda for the upcoming meeting: can we discuss if we want to invite anyone from the outside? Special guest speakers? How are they determined? I didn't know who would be speaking today, and I'd like to either have some input or at least better communication among our members as to what's going on and how we're going to be deciding things.

Dr. Komaroff: This meeting was arranged through "eleventh hour planning" because Dr. Eckert was not yet on the scene to assist.

Dr. Eckert: That is what plagued this meeting. I was a late arrival to this Committee—later than our new members in fact. So I was barred until the *Federal Register* notice came out from contacting the members. That's not going to happen the next time around. I'm going to be going out very shortly with the invitation memo to the Secretary. That will be followed by a copy of the letter to each of you and a recommendation or request of items on the agenda that you would like to see. The *Federal Register* notice will go out earlier next time, and the travel arrangements will be made in a more efficient and more advanced manner. I have the luxury now of having the time to do that, which I didn't have last time.

Dr. Friedman: I'd just like to address the lack of response from HHS to Congressional letters. I don't know if it's standard to ignore them. I think that if a Congressman takes the time to write an inquiry to the Department of Health and Human Services, that Congressperson is entitled to an answer.

Dr. Eckert: I don't know what letters have been sent in; I can check on the progress of a response.

Ms. Healy: We can actually invite representatives of DOD, the Department of Veterans Affairs, the Agency for Healthcare Research and Quality, and the National Institute of Disability and Rehabilitation Research without them being ex-officio members. Our ex-officios just keep giving and giving to us every meeting, but it might be nice to have some fresh perspective and other resources from other agencies to draw upon.

Dr. Komaroff: Would you formally recommend that they be invited to the next meeting? Or would you want to know more about what the agenda was for the next meeting before inviting them?

Ms. Healy: We talked about not moving on to new business until we had resolved old

business, but it might be a positive thing to say, “This is an issue that we are requesting your input on, and we’d like to share what your agency does that might be helpful.”

Dr. Oleske: As a new member, I’ve been impressed with the openness of the discussion with the agencies. Is there a way at the next meeting of having the first half hour set aside for going over the issues that have been discussed? For example, when I mentioned minorities being underserved and found out that the issue had already been discussed many times. Is the issue of the Gulf War veterans in play? My son was in Iraq, came back very damaged, and it took us six months to get him evaluated for post-traumatic stress. I guess I need an introduction about what’s been covered and what topics don’t need to be brought up.

Ms. Healy: Olga could send all past minutes to everyone. I know they’re online because I went over them so that I could be prepared. But I still have a list of questions after reading the minutes on which I need clarification or how the issue was resolved.

Dr. Friedman: Perhaps we could devote the 8-9 a.m. pre-meeting time to a discussion of those issues. That way we can use “open Committee time” for Committee work.

Ms. Artman: What about inviting outside speakers, such as from the VA?

Dr. Friedman: I actually think that they could bring resources because what they do with primary care education, alternative care therapies, and some of the materials that they’re publishing now—they may want to get more involved with supporting this effort. Not just as an ex-officio. May want to get involved in examining a particular group of treatments and how they impact on quality of care.

Dr. Reeves: They have issued a document on chronic fatigue syndrome, so they have people who have been involved. Great idea to invite that agency, but I don’t now how many resources they have to bring to the party.

Ms. Artman: This would give them a chance to do another document on chronic fatigue that might be more to the liking of the community than the first one was. I agree with inviting outside people. We talked before about inviting the Department of Education and other agencies outside of HHS that really could inform us and help in many of the things that we’re doing.

Dr. Robinson: Concerning the issues about children with HIV, with adolescents, etc.—the Department of Education was of particular interest at the time. We did have discussions, there was a presentation by the department, but this panel has not benefited from that.

With regard to the Department of Defense, the Veterans Administration, or any others, again, it would depend on whether or not the panel thought it would be useful information. But there’s no question that Dr. Desi and the people who are responsible for making sure that disability information is available on a daily basis, to me, those are

things that you would assume that you would want to have at every meeting just in terms of reference points for information, for policy, for regulations, and whatever else might be needed.

Dr. Friedman: I would think that the Department of Defense and the Veterans Administration would have an interest in both Gulf War sensitivity and multiple chemical sensitivity, and since there is so much overlap of symptomology between these syndromes and chromic fatigue, I think they would be interested in hearing what we have to offer, and we certainly should be interested in hearing what they have to offer in terms of research capability and also in terms of funding to enhance having more robust research programs for chronic fatigue and related illnesses.

Ms. Artman: Dr. Lapp last year recommended that the Surgeon General also be invited.

Dr. Reeves: I think that if the Secretary can come, that's what we need. This body was originally nested under the Surgeon General, but I believe that's no longer the case. What's the org chart right now?

Dr. Eckert: Unless I'm mistaken, it goes directly from the Executive Secretary to the Assistant Secretary for Health to the Deputy Secretary to the Secretary.

Dr. Robinson: At the time a person was serving as both Surgeon General and Assistant Secretary, so that was consistent with the hierarchy.

Ms. Healy: Why don't we start with one agency and invite the Agency for Health Care Research and Quality since that seems to be the most complementary and we wouldn't have to reach outside the department?

[There was off-mike discussion about inviting at least another of the four agencies that can send representatives without being ex-officio members. Some members noted that both DoD and Veterans Administration have testified before about Gulf War syndrome, so it would not be a big stretch to reach across departments. Members also noted that it is the Committee, not the Secretary, who would issue an invitation.]

Dr. Komaroff: Have any Committee members have individual contacts at the agencies. Dr. Reeves had mentioned briefly in his update that the CDC is working with Fort Benning on a study of infantry recruits washing out of basic training at a rate as high as 20% because they come down with a CFS-like illness. That was suggested as a place to start, given their immediate interest in trying to stem the loss of recruits and the broader issue of other health outcomes that resemble CFS-like illnesses, especially when troops come home from a theatre.

Dr. Papernik: I'm concerned about inviting other departments that are more interested in CFS-like illnesses rather than CFS. I think we muddy the waters by lumping CFS with other syndromes.

Dr. Friedman: Looking at the results of the CDC research, post-traumatic stress disorder seems to be a stress like those in childhood and early adulthood that lead to CFS. I would rather see us have some information and contact on that on a regular basis. Troops coming back from Iraq are exhibiting many of the symptoms that are linked with CFS. I would favor the inclusion of fatigue-like illnesses until we really know what we're talking about.

Dr. Hanna: If you're looking at treatments for post-traumatic stress syndrome, VA is where to get the experts, not DoD. Their treatments are similar to those used for CFS. I would go to the VA for treatment. If you're interested in how DoD philosophically looks at Gulf War Syndrome, I would go to their hierarchy. Know what you're looking for, then find the person knowledgeable about the specific topic.

Dr. Komaroff: Let's focus on what we're inviting them for.

Ms. Healy: After hearing this discussion, I might now propose delaying inviting them until after our next meeting and focus on communicating our ideas to the Secretary. Then maybe we can lay the groundwork for where we're heading.

Committee members generally agreed that this order of activity is reasonable. Dr. Friedman again noted his confusion over where the lines are drawn between CFS and diseases such as Gulf War Syndrome. Dr. Hanna commented that such lines cannot be drawn without markers. She said that Dr. Friedman raises good questions, but they are unanswerable by the Committee.

Dr. Hanna: At NIH the issue is the coding of grants and which receive funding. Much of the basic research applies to a broad number of diseases like CFS, fibromyalgia, etc. No one can draw bright lines between these conditions.

Dr. Komaroff: There are case definitions for both CFS and fibromyalgia, and the relationship between these two illnesses has been carefully studied. There's a big overlap, and many people meet both case definitions. However, a substantial number don't, and meet only one definition or the other. Whether they're separate or just look that way for lack of biomarkers is unknowable at this point.

So it's a political question: should a committee constituted to give advice on CFS be inclusive about pulling in closely related diseases that have their own constituencies or should we focus narrowly on the primary illness in which we have expertise, and where there's a community looking to us to offer leadership?

Debate ensued over these points. Members discussed whether they should be inclusive—since many CFS patients themselves ask to be diagnosed with fibromyalgia in order to get insurance coverage—work only with CFS so that one day it will also be well-defined enough for patients to receive insurance coverage.

Closing Remarks

Dr. Komaroff pointed out that the day's debate over where to draw the disease definition line grew out of which agencies to invite to Committee meetings and asked members to close that loop. Ms. Stevens agreed to defer that decision for another meeting as long as the Committee agreed that it wants to move in the direction of bringing in outside agencies with relevant expertise.

Dr. Friedman noted that he is still frustrated in understanding his charge to advocate for CFS patients in light of the debate over how the disease is defined.

Ms. Fero noted that professionals and patients in the field have the same discussions every day and that the Committee cannot resolve the issues. She said that she wants people to be diagnosed properly and be treated. "A different issue, though, is money. When it comes down to the dollar, I don't want 10 cents of my dollar spent on CFS and the other 90 cents spend on fibromyalgia that excludes CFS. There are so many issues," she concluded. "The Committee is charged with advocating for CFS and should, but beyond that, I don't know the answer."

Ms. Stevens: Our charge is science-based advice on CFS. While we have a lot to learn from these other syndromes, if we get so fragmented from looking at other similar illnesses, we'll never spend any time on our purpose.

Adjournment

A motion for adjournment was made, seconded, and approved by Committee members.