



CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE

Meeting

Monday, May 10, 2010
9:00 a.m. to 4:00 p.m.

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

Agenda Monday, May 10, 2010

9:00 am	<u>Call to Order</u> <u>Opening Remarks</u>	pg 5	Dr. Christopher Snell <i>Chair, CFSAC</i>
	<u>Roll Call, Housekeeping</u>	pg 5	Dr. Wanda Jones <i>Designated Federal Official</i>
9:15 am	<u>Welcome Statement from the Assistant Secretary of Health</u>	pg 5	Dr. Howard K. Koh
	New Members Statement on CFSAC Interests/Goals		CFSAC New Members
10:00 am	<u>Remarks from Dr. Elizabeth Unger</u>	pg 11	Dr. Elizabeth Unger <i>Chronic Viral Diseases Branch, CDC</i>
10:30 am	<u>Blood Safety Update on XMRV</u>	pg 15	Dr. Jerry Holmberg <i>Blood Safety and Availability, Office of Public Health and Science</i>
11:00 am	<u>Review/Update of Past CFSAC Recommendations</u>	pg 20	Committee Members
12:30 pm	<u>Subcommittee Lunch</u>	pg 27	Subcommittee Members
1:30 pm	<u>Public Comment (on CFSAC charter)</u>	pg 27	Public
2:00 pm	<u>Review and Discussion of CFSAC Charter and Bylaws</u>	pg 26	Committee Members
4:00 pm	<u>Adjournment</u>	pg 40	



CHRONIC FATIGUE SYNDROME ADVISORY COMMITTEE

Voting Members

Chair

Christopher Snell, PhD Stockton, CA	Term: 04/01/07 to 04/01/11
Dane B. Cook, PhD Madison, WI	Term: 05/10/10 to 05/10/14
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
Eileen Holderman Galveston, TX	Term: 05/10/10 to 05/10/14
Michael Houghton, PhD Danville, CA	Term: 05/10/10 to 05/10/14
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
Susan M. Levine, MD New York, NY	Term: 05/10/10 to 05/10/14
Gailen Marshall Jr., MD, PhD Jackson, MS	Term: 05/10/10 to 05/10/14
Jason Newfield, Esq. Garden City, NY	Term: 07/01/06 to 07/01/10

Ex Officio Members

Centers for Disease Control and Prevention

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

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

Food and Drug Administration

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

Health Resources and Services Administration

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

National Institutes of Health

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

Social Security Administration

Cheryl A. Williams (*Primary*)
Acting Director
Office of Medical Listings Improvement

Mike O'Connor (*Alternate*)
Supervisory Team Leader
Office of Medical Listings Improvement

Executive Secretary (Designated Federal Official)

Wanda K. Jones, DrPH
Principal Deputy Assistant Secretary for Health
Office of Public Health and Science

Monday, May 10, 2010

The following document contains highlights of the Chronic Fatigue Syndrome Advisory Committee (CFSAC) Meeting held on May 10, 2010. Access a podcast of complete meeting proceedings at: <http://www.hhs.gov/advcomcfs/>.

Call to Order/Opening Remarks

Dr. Christopher Snell

- Welcomed meeting attendees; stated that he is honored to serve as CFSAC chair and take part in the committee's important work.
- Stated that CFSAC members are humbled in front of patient groups that attend meetings and declared that the committee will do its best to serve the CFS population.
- Noted the exciting scientific developments in the CFS field over the past year and expressed hope that CFSAC can help push those developments forward.

Roll Call, Housekeeping

Dr. Wanda Jones

- Noted that CFSAC has five new members, with a sixth scheduled to be sworn in when Jason Newfield's term ends on July 1. Informed the committee that the future member is in attendance as a special expert and plans to participate in subcommittee meetings as soon as his term begins.
- Pointed out each new CFSAC member during roll call.
- Noted that Kevin Parmer is substituting for Cheryl Williams as the Social Security Administration (SSA) *ex officio* representative.
- Announced that Christine Williams from the Agency for Healthcare Research and Quality (AHRQ) is attending the meeting as a special expert. Dr. Jones noted that CFSAC members have expressed long-term support for adding AHRQ as an *ex officio* agency.
- Explained building, security, and cafeteria logistics, including the need for members of the public to have an HHS escort when moving throughout the building and the availability of staff to serve as escorts throughout the day.

Welcome Statement from the Assistant Secretary for Health

Dr. Jones introduced Dr. Howard K. Koh, noting that he took over his post as Assistant Secretary for Health almost a year prior to the meeting. She said that Dr. Koh became interested in CFSAC early in his tenure, but his schedule did not permit him to attend the fall meeting. She said that he has made a commitment to become more

engaged in ensuring that CFSAC recommendations receive proper consideration and that members receive HHS feedback.

Dr. Howard K. Koh, Assistant Secretary of Health, HHS

- Welcomed meeting attendees and thanked CFSAC members for their service. Dr. Koh said that HHS relies on committee members sharing their time, expertise, and passion to help the country be healthier.
- Noted that he had just had the honor of swearing in five new CFSAC members.
- Described himself as a board-certified physician in four areas whose career has given him a broad prospective on health issues. He began his 30-year clinical career in Boston, where he was a researcher at Boston Hospital and Harvard School of Public Health. Dr. Koh served as the Massachusetts Health Commissioner from 1997-2003.
- Told members that he is humbled when meeting advisory committee members because of the cutting edge knowledge that allows them to teach and advise HHS officials in many areas.
- Thanked Dr. Jones for informing him about the importance of CFSAC's work and updating him about scientific developments, including the 2010 XMRV conference scheduled for the fall and the NIH CFS state of the knowledge conference scheduled for 2011. Dr. Koh said that he wanted to work closely with CFSAC on making the conferences relevant to the people swerved by HHS.
- Noted that the knowledge and experience of **Dr. Jerry Holmberg**, HHS senior advisor on blood safety, are integral to the work of the Office of the Assistant Secretary of Health.
- Asked that CFSAC members introduce themselves and describe their involvement with CFS:

Leonard Jason – Professor of psychology at DePaul University; Director of the Center for Community Research; involved over the past 15 years in epidemiology and diagnostic issues associated with the case definition of CFS.

Gailen Marshall – University of Mississippi Medical Center. Has researched and cared for patients with immune-based diseases for 25 years. Interest in and expertise on CFS is related to the fact that it is not a single disease entity, but has multiple ideologies and therefore needs multiple, organized approaches to care.

Nancy Klimas – University of Miami and Veterans Affairs in Miami. Has been in the field for more than 20 years doing both patient care and clinical and basic research on CFS and Gulf War illness.

Michael Houghton – His laboratory discovered the Hepatitis C virus in the late 1980s after which it developed blood tests, identified blood targets, and developed vaccine strategies for clinical testing. Has turned his interest toward CFS in the last several years and will be joining the University of Alberta in Canada this summer to initiate research in the field.

Susan Levine – Clinician in New York City where she has cared for patients with CFS for 20 years.

Marc Cavaille-Coll – Food and Drug Administration (FDA) *ex officio* CFS member, Division of Special Pathogens and Transplantation Products at the Center for Drug Evaluation and Research. Has worked with the advisory committee since its creation.

Eleanor Hanna – National Institutes of Health (NIH) *ex officio* member, Office of Research on Women's Health. Has worked with CFSAC since 2001.

Christopher Snell – Professor and Department Chair at the University of the Pacific in Stockton, CA where a research group with an interest in energy metabolism fatigue has been involved in CFS research for 12 years. Has been a CFSAC member for three years.

Mike Miller – Centers for Disease Control and Prevention (CDC) *ex officio* member, Associate Director for Laboratory Science for the newly named National Center for Emerging and Zoonotic Infectious Diseases. Trained as a clinical microbiologist who has been at the CDC for 37 years and a CFSAC member for two years.

Deborah Willis-Fillinger – Practicing internist for 27 years and on the HRSA staff for 20 years, where she is currently Acting Director for the Office of Health Equity. Has served as HRSA *ex officio* representative for three years.

Chris Williams – Director for Strategic Partnerships at AHRQ; formerly Director of the Office of Communications and Knowledge Transfer. Experienced in translating research into practice for clinicians, health systems, and other audiences. Prior to her executive branch career, she spent 13 years as health policy advisor to former Senate Majority Leader George Mitchell. Ms. Williams is a CFS patient.

Mike O'Connor – Social Security Administration (SSA) *ex officio* member, Office of Disability Programs, which is responsible for the medical and disability policies surrounding CFS.

Kevin Parmer – Alternate SSA *ex officio* member, Office of Disability Programs, attending for Cheryl Williams.

Jason Newfield – New York attorney advocating for patients' long-term disability claims. Has been a CFSAC member since 2006.

Dane Cook – University of Wisconsin—Madison in the Department of Kinesiology with an interest in the psychobiology of fatigue and pain.

Ron Glaser – Head of the Institute for Behavioral Medicine Research at Ohio State University Medical Center. Works most closely with his clinical psychologist wife. Glaser is a tumor virologist with an interest in Epstein-Barr virus, viral latency, nasopharyngeal carcinoma, and how stress affects the immune system. Has worked with Nancy Klimas and Gailen Marshall for many years; published first paper on CFS with Jim Jones at the CDC.

Arthur Hartz – University of Utah; Director of Health Services Research at Huntsman Cancer Institute. Research interest is identifying patient factors that are associated with the prognosis of CFS and interventions that alter the disease course.

Eileen Holderman – Patient advocate from Galveston, TX. Has been trustee for the New Jersey CFS Association and a contributor to the organization's media relations and public policy.

Dr. Koh

- Remarked that CFS raises “critically important issues” and “is a public health issue in its broadest sense.” He commended the commitment and perseverance of CFSAC members, who began tackling CFS on behalf of patients without complete knowledge of etiology or cause.
- Told committee members that “we’re hoping that this new administration can work more closely with you on CFS as we move forward...We are committed to continuing the momentum here.”
- Called for a round of applause for Dr. Jones; said that he has lost track of the number of times during his beginning months when she briefed him on the importance of CFS issues.
- Noted that he and Dr. Snell spoke over the phone in anticipation of the meeting, thanked Dr. Snell for his service, and called for a round of applause.
- Said that he wants to attend as many advisory committee meetings as possible and is looking forward to upcoming opportunities including the XMRV fall meeting and the 2011 NIH state of the knowledge meeting. He expressed hope that reviewing the science will lead to better defining the etiology and easing the suffering of people living with CFS.

- Set a goal for next CFSAC meeting of reviewing and taking action on some of the committee's past recommendations. Acknowledged the time and energy that CFSAC members put into the recommendations. Commented that while some pose resource and logistical challenges, others can be moved on promptly.
- Commented that the passage of health reform has the potential to make the US health system a true health system, perhaps for the first time ever. During this "incredible time," HHS is implementing reform on literally dozens of fronts, including improving patient care, focusing more on the medical home, placing added emphasis on prevention, taking care of the whole patient, and building public health so that people do not become patients in the first place.
- Noted his intention to brief the HHS Secretary on behalf of CFSAC and encourage her to visit the committee in the near future.

Committee Discussion

Dr. Jason acknowledged Dr. Jones for instituting the webcast of CFSAC meetings. He then asked Dr. Koh to explain the mechanism for delivering committee recommendations to the Secretary, including how decisions are made on whether or not to take action.

Dr. Koh noted that HHS has 150 advisory committees. All of them regularly produce recommendations and all recommendations get reviewed. What has not happened—and what needs to be improved—is direct face-to-face communication back to CFSAC on which recommendations can be acted on immediately and which need more time, said Dr. Koh. He made the commitment to improve such face-to-face feedback.

Only 15 percent of CFS patients have been diagnosed due to lack of access to knowledgeable healthcare providers, said Dr. Klimas. The result is tremendous suffering. Because of this, CFSAC has repeatedly recommended creating regional centers where experts can gather for a clinical team-building effort aimed at increasing the momentum for establishing clinical guidelines and effective therapies. If the committee could achieve that, it would achieve a tremendous service for the patients, concluded Dr. Klimas.

Dr. Koh told the committee that he and Dr. Jones had a direct discussion about the issue with Dr. Francis Collins, the new NIH director. Dr. Koh commented that the creation of a center is "so, so reasonable."

Dr. Hartz asked what kinds of CFSAC recommendations are most useful. Dr. Koh replied that addressing patient need is the place to start with any public health issue. He remarked that in the current tough economic times, recommendations that do not require large resources are easier to push along faster, but that the focus must be on the need.

Dr. Snell emphasized that it is key to CFSAC members to get feedback on their recommendations and that anything that Dr. Koh can do to increase feedback will be greatly appreciated.

Housekeeping

Dr. Jones added the following housekeeping items:

- A reminder to set electronic devices to vibrate or mute.
- A discussion of the state of the CFSAC charter and why the committee is having a one-day meeting. She and her staff had to consider the following factors:
 - The fall XMRV conference and the NIH state of the knowledge meeting in 2011, which offer the opportunity for CFSAC to be visibly present.
 - The “considerable uncertainty” in January and February when no news was forthcoming about progress in approving nominees to replace outgoing CFSAC members. Dr. Jones noted that advisory committee members go through a selection process that is almost as extensive as the one for Presidential nominees.
 - Dr. Koh’s busy schedule.
 - The need to consider charter issues (such as the committee’s purpose and adding AHRQ as an *ex officio* member) rather than rubber stamping the current charter, which runs out in September.
- Dr Jones decided to schedule a one-day meeting to address urgent issues while conserving resources for possible future opportunities, such as CFSAC members attending upcoming science meetings. She explained that the CFSAC annual budget has been increased from \$100,000 to \$130,000, with the bulk of funding going to webcasting and members’ travel. Dr. Jones maintained that the committee will benefit from a one-day meeting to take up the charter while still preserving the possibility of a CFSAC presence at the fall XMRV conference.

Dr. Jason asked about the possibility of staggering the terms of CFSAC members to avoid the discontinuity of the current situation in which almost all members are ending their term within a year.

Dr. Jones replied that her staff has mapped out a plan that will see only two or three members turnover at one time by 2015. CFSAC would not be in danger of losing a quorum during any one turnover cycle. The staff would also be constantly soliciting new members and sending their nominations forward for vetting. Dr. Jones explained that for the current round of nominees, all information was gathered by Thanksgiving 2009, but the initial nomination package underwent about 100 days of vetting.

Dr. Snell said that he has volunteered to extend his term by a year if necessary and can look into extending one or two other people's terms in order to provide continuity to new members.

Dr. Jones thanked Dr. Koh for his time and said CFSAC will promptly deliver its recommendations to his office.

Update on CDC's CFS Public Health Research Program

Dr. Elizabeth Unger, Acting Chief, *Chronic Viral Diseases Branch (CVDB), CDC*

Please note: The following section highlights key points made during the presentation. Access to any presentation text and accompanying documents is available at: <http://www.hhs.gov/advcomcfs/meetings/presentations/05102010.html>.

Dr. Miller introduced Dr. Unger as the new acting leader for the chronic fatigue group at CDC. He described her as an MD who has been at CDC for 13 years and a PhD researcher of international reputation who is bringing a wealth of experience to the position. She is the acting branch chief of a newly named division under CDC reorganization called the Division of High Consequence Pathogens and Pathology, which includes Ebola, anthrax, small pox, and other high-consequence diseases.

Dr. Unger assured the committee that the CDC CFS public health research program is moving forward, and then addressed the following topics:

New Laboratory Space

- CFS and HPV research will be moving in June to a new building that offers a "significantly enhanced environment."

New Publications

The CDC is committed to publishing its findings in peer review literature. Nine publications have appeared in print or e-publication in advance of print since the October 2009 CFSAC meeting. These include:

- A study in which participants with CFS were twice as likely as healthy controls to have metabolic syndrome. For participants with CFS, the number of metabolic factors correlated with the increasing severity of fatigue. The study emphasizes the need to evaluate and manage metabolic syndrome in those with CFS.
- A study that presents survey data collected from convenience and probability samples to fill in the evidence base of US Healthcare providers' knowledge, attitudes, and beliefs about CFS. Data provide a benchmark for metrics to evaluate the success of ongoing educational efforts.

- Formal validation of the multidimensional fatigue inventory (MFI) instrument in a US population. These data are needed to support ongoing efforts to reliably measure domains of CFS.

Study Updates

Field work on three large studies have been completed: the follow-up study of CFS and chronic unwellness in Georgia, the pathophysiologic mechanisms of CFS, and the pilot registry of CFS. Data cleaning and lab testing are ongoing.

Five-Year Strategic Plan

During this time of transition at CDC, it is useful to have a guide to assure forward momentum in CFS public health initiatives, said Dr. Unger. The five-year plan is, however, a living document, and CDC will continue to adapt as needed to optimize the impact of the program in a changing environment.

This program is not the vision and work of one person, she said. It is the result of a group of dedicated scientists and administrators committed to conducting research that leads to control and prevention strategies for CFS, reducing the morbidity associated with the disease, and improving the quality of life for those suffering with CFS and their families.

Committee Discussion

Dr. Jason thanked Dr. Unger for her brevity, a request that CFSAC has made to all presenters. He noted language in the five-year plan about interacting with the larger scientific community and asked Dr. Unger for her vision of how this collaboration will occur. She replied that improving communication with the academic community at large is “one of most important tasks we have” and that the CDC is considering what the optimum actions would be, including conferences. She said that the CDC is “still very much in the transition phase” and has not made concrete plans.

Dr. Hartz asked whether Dr. Unger has considered research collaboration with a wider range of scientists, including data sharing.

Data availability – Dr. Unger replied that the CDC understands the importance of making its valuable data most useful to the research community. The agency is working on an approach through a special CFS data center that uses the appropriate annotation and controls but also makes the data useful and publicly accessible. She added that accomplishing the process is a commitment of resources, so the CDC will probably move too slowly for outside interests, but “we are doing it judiciously.”

Research collaboration – The next series of data being explored will direct the CDC to the most promising areas, said Dr. Unger, and the agency fully intends to reach out to the academic community for its support in expanding the agency’s work. She

acknowledged that CFS research presents multi-disciplinary challenges and the CDC does not have all of the experts within its community.

Dr. Snell asked Dr. Unger to comment on the empirical definition of CFS used by the CDC. She acknowledged the CDC's failure in communicating how it uses the definition and said that it should not have been labeled "empirical" because it is the same as the 1994 international case definition.

Dr. Unger said that as the diagnostic criteria is more objectively applied, the CDC is making some decisions that need to be validated and presented to the community at large. The first priority, said Dr. Unger, is presenting permutations of cutoff criteria gleaned from the follow-up of the Georgia surveillance population study and how these criteria would affect which patients are classified as having CFS. Once this occurs, she said, it will be clear whether a meeting is needed to further debate issues related to the case definition.

Dr. Klimas asked what the CDC's next direction will be when the completion of field work frees up budget dollars that were devoted to those studies. Dr. Under replied that her office is in the process of finalizing plans for this fiscal year and that she will be working with her group to determine what to do next. Options include a second follow-up in the Georgia surveillance.

Ms. Williams asked Dr. Unger to elaborate on the pilot registry. Dr. Unger noted that the full name is the Registry of Unexplained Fatiguing Illnesses and Chronic Fatigue Syndrome. It was started with the purpose of understanding how a registry for CFS would work. The CDC also used the registry as a way to educate healthcare providers who would be referring their patients.

The CDC enrolled 825 healthcare providers—both physicians and non-physicians—practicing in Bibb County and the surrounding area, making it a population-based referral, Dr. Unger explained. CDC staff educated the providers about CFS and encouraged them to refer patients who met the criteria to be evaluated. Each referral completed the same questionnaire and had a clinic visit to evaluate for CFS criteria just as in the CDC's other surveillance studies. Toward the end, the CDC consulted with a patient advocacy group in Bibb County and allowed members to self-refer. The CDC has just completed that enrollment. Questions include:

How cost effective was this method of enrollment?

What are other options for doing a registry?

Preliminary data evaluation indicates that patients from the advocacy group have a lot more associated illnesses than those referred from physicians' offices.

Ms. Williams noted that AHRQ is interested in patient registries and has developed a how-to handbook to assist health systems.

Dr. Jason expressed appreciation for Dr. Unger's openness with the committee and said that it indicates a promising new relationship with the CDC. He asked her to comment on what she sees as her relationship with the CFSAC, whether the CDC still maintains that there are four million people with CFS in the United States, and what mechanism is in place for selection of a permanent person for her position.

Dr. Unger replied that in the process of reviewing the "nitty gritty" workings of the CFS case definition, her office will also revisit the total patient number. She noted that she was involved in the decision during the CDC's original surveillance to try to broaden the criteria for looking at patients with the potential diagnosis of CFS. From everything that was learned about CFS, it appeared that a focus on only fatigue missed people who fully met the case definition, said Dr. Unger. The process must also ensure that it does not include people who do not have CFS. So far, said Dr. Unger, she stands by the CDC's number.

She added that the process of permanently filling her position is underway and making progress. In the meantime, she said that she attended the current CFSAC meeting to try to better understand its work and determine how the committee and CDC can have a productive interaction.

Dr. Hartz asked Dr. Unger to explain what the CDC is trying to learn with its registry. Dr. Unger replied that she is not primarily responsible for the registry and cannot give a completely adequate answer, but noted that part of the purpose is to follow patients through time to understand how CFS progresses and observe other illnesses that may intervene.

Dr. Hartz asked why the registry was limited to one county. Dr. Unger replied that it allowed the CDC group to understand the workings of a registry, since the group had not done one before. The research allowed the group to see what did and did not work, how much information could be gleaned from a registry, and whether and how to expand it. Dr. Hartz asked whether patients in the registry can be pulled for laboratory and other types of studies. Dr. Unger said that the intention was to be able to contact patients again for potential participation in other research studies. The current contract for the registry has ended and the CDC is deciding how to move forward with it.

Dr. Klimas inquired whether the data has produced obvious subgroups. Dr. Unger said that her group is trying to focus on biologic measures that could stratify groups. An example is the Trier Social Stress test, which sometimes produces a blunted cortisol response.

Dr. Jason asked Dr. Unger to comment on using exercise a stressor as opposed to other methods and qualifying patients as disabled with CFS through criteria based on emotional disorders. Dr. Unger said that her group is looking at all of the instruments and cutoffs used and how they affect who does and does not meet the definition of CFS. She added that the CDC gleaned some interesting information from the exercise challenge; then the decision was made to try a different kind of challenge. This is not to

say that exercise is not a good challenge, she said. Researchers want to see CFS in motion; a static picture is harder to understand than observing responses.

Dr. Miller concluded by introducing **Dr. Kimberly Hummel**, who works with the Chronic Viral Diseases Branch as Associate Director for Laboratory Science in the Division of High Consequence Pathogens and Pathology. She also works with the policy components of CFS and has been kept up to date with CFSAC activities.

Blood Safety Update on XMRV

Jerry Holmberg, PhD, Senior Advisor for Blood Policy, *Blood Safety and Availability*, Office of Public Health and Science (OPHS)

Please note: The following section highlights key points made during the presentation. Access to any presentation text and accompanying documents is available at: <http://www.hhs.gov/advcomcfs/meetings/presentations/05102010.html>.

Dr. Holmberg stressed the high level of coordination within HHS that is being directed by his office to try to ensure the safety of the blood supply during the investigation of XMRV/CFS.

He explained his responsibility for blood safety and availability as:

- Coordinating the HHS response.
- Understanding XMRV detection, prevalence, and epidemiology.
- Preventing disease transmission through blood and blood products if XMRV is found to be disease-causing in humans.

Since November, Dr. Holmberg's office has been:

- Looking into the standardization and validation of different detection methods.
- Conducting epidemiology studies to determine prevalence.
- Developing risk assessment and risk management plans for controlling XMRV.

As Senior Advisor for Blood Policy, Dr. Holmberg is coordinating the following elements:

- Blood Organ Tissue Senior Executive Council, the senior leadership from public health services.
- Monthly Blood Organ Tissue Safety, a monthly call with working level staff involved in blood organ and tissue safety.
- Emerging Infectious Disease Working Group, a standing committee that reports on a monthly basis.
- XMRV Scientific Research Working Group, created in reaction to the XMRV report in *Science* magazine.

- American Association of Blood Banks (AABB) XMRV Task Force. AABB has created a group of experts inside and outside of government who can address XMRV/blood supply issues. The task force is headed by Dr. Harvey Klein, Chief of the Department of Transfusion Medicine at the NIH Clinical Center. Dr. Klein is also working with Dr. Holmberg on the monthly blood organ and tissue safety calls and the executive council. The AABB task force and XMRV working group are in contact almost daily and have a standing lengthy phone call at least once every two weeks.

Dr. Holmberg introduced **Dr. Simone Glynn**, Director of Blood Resources Program at the National Heart, Lung, and Blood Institute and co-chair of the Blood XMRV Scientific Research Working Group. Dr. Glynn oversees the Retrovirus Epidemiology Donor Study (REDS) established in early 1990s. REDS 2 is scheduled to conclude in December 2010, with REDS 3 scheduled to begin soon after.

Blood XMRV Scientific Research Working Group Activities

Quantitation Phase (December-January 2010)

- Quantitation of cell lines that were available.
- Six government and private laboratories signed up to participate, including the Whittemore-Peterson Institute (WPI).

Analytical Panels (distributed in March 2010)

- Begun after quantitation of the number of viral copies in the cell or the supernate.
- Developed 15 panels based on the number of laboratories that expressed interest both in and outside the United States.
- Cell line used was human prostate 22Rv1.
- Six labs are participating—the CDC, FDA (2), National Cancer Institute (NCI), WPI, and Blood Systems Research Institute (major contractor for the REDS 2 study).
- Most results are in; a few are expected in June.

Pilot Studies to Address Problems

- Delayed by institutional review board (IRB) process. Scheduled to begin in the June/July timeframe.
- Must identify the processing time between the collection and preparation of the samples.
- Must identify the differences between the whole blood preps and the peripheral blood mononuclear cells.
- Two neutral individuals will be collecting results for the analytical and the clinical panel, then report results to the working group.

Clinical Panel

- Again, had to wait for IRB approval for taking samples from 25 CFS patients.
- Plasma and whole blood panels will be matched.

Serological Assays

- NCI is developing antibodies.
- At least one commercial source is working on the methodology.
- Once these methods are put into place, it will be necessary to standardize them with the analytical and clinical panels.

Publications

After the positive XMRV results reported in the October 2009 *Science* magazine, three reports with less positive results followed in January/February 2010, according to Dr. Holmberg. He noted, however, that once procedures are standardized, study-to-study comparisons will be more useful. He added that his office continues to keep up with research findings from around the world.

Epidemiological Findings (after standardization)

What is known today...

- Confounding association between XMRV and CFS.
- No epidemiological association has been demonstrated with blood transfusion.
- Confounding association between XMRV and familial prostate cancer.
- The prevalence of XMRV in blood donors is not known at the present time, although the *Science* paper reported a 3.7 percent prevalence. The goal of ongoing study is to accurately determine the prevalence in the donor population.

From international scientific literature...

Prostate Cancer

- Two Japanese studies using the same cohorts reach two different conclusions about the association of blood transfusion with prostate cancer. The first study finds a correlation with cancer, but not prostate cancer, and the second finds a correlation with prostate cancer.
- A larger study from Sweden [using 28,000 non-transfused patients and 1,500 transfused patients from 1981-1991] found no relationship between prostate cancer and transfusion.
- One of the biggest studies that has ever been funded by NIH showed no relation between transfusion and the onset of prostate cancer.

Current Blood Donor Screening Status

There are safeguards in place.

- The AABB standard states that “the prospective donor shall appear to be in good health and shall be free of major organ disease, cancer, or abnormal bleeding tendency, unless determined eligible by the medical director.”
- The Code of Federal Regulation that addresses the suitability of donors as a source of Whole Blood requires that suitability be determined by a qualified physician or by persons under his/her supervision who are trained in determining suitability. Donors may not serve as sources of Whole Blood more than once in eight weeks and must be in good health as defined by a set of criteria.
- AABB approved a unified donor questionnaire in October 2006. The first question asks if the donor is “feeling healthy and well today.”
- If there is any reason to doubt the health of a donor, that person should be further questioned by the medical director.

Other countries have moved forward with deferral of blood donors:

- The Canadian blood service (not Hema-Quebec) has instituted an indefinite deferral for donors with a history of CFS. Hema Quebec has taken a wait-and-see position. There is no specific screening question.
- The Australian Red Cross has implemented a two-year moratorium on accepting blood donors with a history of CFS but has no screening question. Previous policy was to defer donors only for active CFS.
- New Zealand has changed its policy from indefinite deferral for active CFS to indefinite deferral for a history of CFS, with no screening question.

The OPHS working group is looking into strategies for having procedures in place to mitigate the risk if it is proved that XMRV is a causative agent for disease in humans.

Communications

- XMRV questions and answers posted on CDC website.
- Have consulted with NIH and FDA on the wording of website postings.
- The CFSAC site links to the CDC Q&A:

Q: Should an individual with diagnosed CFS donate blood?

A: At the present time, there are no specific recommendations to defer donors who have CFS. However, FDA regulations require that a donor should be in good health.

Medical Directors at blood collection centers should exercise judgment in determining whether individuals with a history of CFS are in good health at the time of donation.

- Q&A has also been posted by NIH on the NCI website.
- In August 2009, the AABB Transfusion-Transmitted Disease Committee created a color-coded system of identifying infectious diseases that could pose a threat to the blood supply and in April 2010 released an updated XMRV fact sheet that includes the latest journal citations.
- As new developments occur, the OPHS task force will make the information available to the CFSAC website and other links.
- Coming September 7-9, 2010 to the NIH Lister Hill Center Auditorium—1st International Workshop on XMRV: Pathogenesis, Clinical, and Public Health Implications. The organizing body is Virology Education in the Netherlands.

Committee Discussion

Investigators who want to request antibody serum samples must place a request through Dr. Glynn at NHLBI or with NCI.

CFSAC members discussed the issues surrounding CFS patients donating blood:

- CFS patients are already known to be donating blood.
- Many committee members favored erring on the side of safety and eliminating blood donors with a history of CFS.
- Infectious diseases, including CFS are cyclical in nature. Symptoms wax and wane dramatically and unpredictably. Feelings of wellness cannot be relied upon, especially if there is a retrovirus involved.
- CFS patients already have low blood volumes and should not be donating blood.
- The etiology of CFS and its association with XMRV may not be known for another five or ten years.
- CFS results in some of the most seriously disabled patients compared to almost any other condition. How can one ever justify defining CFS patients as a healthy group?
- [Dr. Holmberg] The blood bank community must be aware of discussions going on with patient groups and scientific bodies as the epidemiological research moves forward.
- [Dr. Holmberg] While screening donors by asking questions is extremely difficult, a mechanism could also be put in place to educate donors about CFS.
- CFS patients would voluntarily stop giving blood if they were adequately warned of the possible negative impact.
- XMRV is only the latest infectious agent associated with CFS, not the first.
- [Dr. Holmberg] Research is underway in the United States to discover pathogenetic agents to add to the blood supply and blood products to kill potential pathogens so that those responsible for blood supply safety are not constantly chasing the next pathogen.

- Dr. Holmberg described the difficulties that have arisen during discussions with the blood bank community about deferring CFS patients:
 - Sorting through the confounding data.
 - Lack of information on the epidemiology. XMRV exists and it would be foolish to say that it is not transmitted by blood. What is not known is whether it causes disease in humans.
 - Until the epidemiology is known, educational materials could be distributed to express concern over transmission by blood transfusion. The task force is working on different approaches for this.
- [Holmberg] Although it is not possible to quantify how many donors would be lost by deferring CFS patients, it is unlikely to seriously impact the blood supply.
- [Holmberg] The US blood supply is not controlled by the Federal government. Most of the supply is controlled by the Red Cross and community blood centers. The task force is discussing these issues with blood bank organizations in the absence of a definitive epidemiological association between XMRV and CFS.

Review/Update of Past CFSAC Recommendations

Dr. Jones informed committee members that **Dr. Koh** has seen the chart of “CFSAC Recommendations Since September 2004” and “wants the Department to do better” with their implementation. As with other advisory committees’ recommendations, there are multiple reasons for lack of progress in implementation. These reasons might include the item being beyond the Department’s mission, not strictly a Federal responsibility, or unable to be implemented according to the language as proposed.

“We want to get to ‘Yes’” on all recommendations,” Dr. Jones said. She explained that while the official tally on the committee website shows progress on 18 percent of CFSAC recommendations, that success rate is actually higher. The 18 percent figure was calculated before creation of the chart as a standardized method of reporting progress. Some areas of progress include:

- The NIH 2011 state of the knowledge conference on CFS.
- CDC progress in completing field research work, beginning data analysis, and making changes in leadership.

Dr. Jones noted that CFSAC is seeking to make more progress despite flat or declining budgets and a policy shift from an emphasis on chronic infectious diseases to bioterrorism and homeland security.

Blood Supply Recommendation

CFSAC members suspended their discussion of past recommendations to take up the following motion offered by **Dr. Jason**:

Given the concerns for patient health, including blood volume, and given the fact that we do not know what virus or retrovirus is involved, it is prudent to recommend that individuals who have a diagnosis or a prior diagnosis of CFS not to donate blood.

Committee Discussion

CFSAC members discussed issues raised by the recommendation:

- How will the subject of CFS be presented to donors—as a screening question or as something that must be volunteered?
- Not many people severely ill with CFS will be walking through the door to donate blood. Volunteers are likely to be those with a history of CFS or those people with the disease in remission. People could be asked the question and given an information sheet explaining why blood donation is not a wise idea for the patient or the blood supply.
- CFS patients would already be donating blood as a way to do something for their fellow human beings. They are unlikely to lie about having a history of CFS.
- Questions about general wellness are vague and subjective enough that a CFS patient could filter through the screening.
- Eighty-five percent of CFS patients are undiagnosed. An information brochure could be handed out to donors, who would then be asked if they think they ever had the illness.
- No one question will filter out the undiagnosed CFS population. People would have to be presented with the eight criteria and asked if they have ever had three or more of those symptoms.
- There is a problem with the accuracy of people self-diagnosing CFS, especially when they do not really know what it is. People think that if they have been tired, they have had CFS. Self-screening may lose a lot of donors.
- Deferring patients with a diagnosis and history of CFS would be a good start. The publicity attracted by deferral would present a good opportunity to educate providers and the public. The public education possibilities are enormous both within and outside of the United States.

Dr. Snell offered the following friendly amendment to Dr. Jason's motion: Recommend to the Secretary that he ask that the blood supply indefinitely defer from giving blood people with a history of CFS and that a CFS screening question be added.

- **Dr. Hanna** stated that until more is known about the existence and prevalence of XMRV in the blood supply, NIH's position is that the agency is waiting for answers. Unanswered questions included, does it exist in the blood supply, what is the prevalence, and is there going to be an association in these epidemiological studies? If answers are coming soon, does CFSAC want to create a scare before there's a need for it?
- The scare is already out there, several members said. The issue of CFS patients giving blood goes beyond XMRV, which is just the latest virus. EBV has been

around much longer. Those living with this disease are very sick and there are multiple reasons why they should not be giving blood.

- Dr. Holmberg was asked to talk about the negative aspects of deferring CFS patients until it is known whether or not they have an infectious agent that can be transmitted through blood, and he did not present any negative points.

CFSAC unanimously passed the following recommendation: Given the concerns for patient health, including blood volume, and given the fact that we do not know what virus or retrovirus is involved, we recommend to the Secretary that she ask the blood suppliers to indefinitely defer from giving blood those people with a history of CFS, and that a CFS screening question be added.

CFSAC members then resumed their review/update of past recommendations.

State of the Knowledge Meeting

Dr. Hanna informed CFSAC members that she will be asking them to take part in the planning and presentations for the 2011 CFS State of the Knowledge Meeting. She informed members that she has been speaking with **Ms. Williams** about whether and how AHRQ will contribute to the meeting. Dr. Jones noted that the 2001 AHRQ document entitled *Defining and Managing Chronic Fatigue Syndrome* is available from the CFSAC online archive.

Mr. Newfield inquired about CDC plans for an international CFS workshop, originally scheduled for winter 2009. **Dr. Unger** replied that CDC's reorganization has disrupted the schedule and that the workshop is now being planned for fiscal year 2011. She said that a 2011 workshop will be timelier because the CDC will have data from the Georgia surveillance study and the metrics that reveal various permutations.

SG Letter to Practitioners/Institutions

Dr. Klimas noted that:

- CFSAC recommendations fall into three financial categories—those that cost money, those that redirect money, and those that cost no money at all.
- New CFSAC members may not have understood when reading the recommendations chart that the centers of excellence recommendation appears more than once because it has been a primary concern since the creation of the advisory committee.
- The committee recommended in 2007 that the Surgeon General (SG) send a letter to state health departments, educational institutions, and other medical organizations informing them of CFS educational resources. Dr. Klimas asked whether that recommendation could be resurrected and acted upon. Dr. Jones suggested that a letter might be more effective if it came from the Assistant Secretary for Health, who is the SG's supervisor and is more commonly in touch with state and local health officials.

Dr. Hanna noted that the letter has been drafted but never sent. Dr. Klimas suggested that a CFSAC subcommittee should resurrect the letter and decide how to proceed.

Centers of Excellence

Dr. Jason expressed concern that the listed recommendations represent a variety of separate items with no strategic plan in place to effect policy in a focused way. He suggested that CFSAC might be more successful by better targeting what it wants to accomplish. Mr. Newfield noted that CFSAC may want to move from broad recommendations to “taking smaller bites” and accomplishing the items that do not require significant resources. Dr. Jason commented that “targeted” need not necessarily equate with “small”—CFSAC can tackle large issues and set the bar high.

Dr. Levine said that she would want to know “the nitty gritty” involved in defining and developing centers of excellence. She said that there is a need for centers, noting that no facility exists on the East Coast to which she can refer CFS patients for primary or specialty care. Dr. Snell acknowledged that and said that although private US organizations have developed centers, CFSAC has not yet worked on the specifics of what a center would look like.

Dr. Marshall said that patients and clinicians would want to focus on cutting edge care while researchers would want to focus on the science. He acknowledged that a center is a large undertaking and Dr. Koh advised that recommendations with no resource requests will move faster. CFSAC can show, however, that although centers are expensive, the short- and long-term benefits to patients and the public provide a reason to spend the money.

Dr. Snell suggested that the most effective course is for CFSAC to organize and prioritize desired actions before conducting a dialog with Dr. Koh. Dr. Jason noted that Dr. Koh encouraged CFSAC to first consider the greatest need. That should help the committee prioritize recommendations.

Dr. Klimas summarized that 85 percent of CFS patients are undiagnosed, patients suffer a tremendous lack of access to clinicians and care, and research progress is seriously hampered because scientists do not have access to the patient population to study it in an organized fashion. Even though centers may be the most expensive item on the recommendations list, they should be a top priority.

Ms. Williams suggested that CFSAC consider what infrastructure already exists in the public or private sector. AHRQ has two research networks that integrate research and practice. One is a primary care network made up of primary practices and the other is an integrated health research network. The goal is to discover how research can be integrated into the practice of medicine and what can be learned from practicing physicians. She urged CFSAC to consider using one of the AHRQ networks or a similar

model, noting that the agency has five or six years experience in bringing together research with the practice of medicine.

Dr. Snell noted that CFSAC could also take advantage of the government's current concern with access to healthcare by underserved populations. Dr. Jason inquired whether any existing synergy between AHRQ and HRSA could be used to further the work of the committee. **Dr. Willis-Fillinger** said that the two agencies have worked in the past on health disparities and are currently discussing collaborating in the future. She suggested that practice guidelines might be an area for joint HRSA/CFSAC collaboration, starting with how the guidelines that already exist play out in actual practice.

Ms. Williams noted that AHRQ is the "science partner" in collaborations with HRSA. AHRQ does not regulate or pay for patient care. AHRQ has many partners in the private healthcare delivery system and partnering with HRSA would move activities to the public side and bring in a lot of patients.

Dr. Jason asked Dr. Willis-Fillinger why HRSA is not already involved in various activities discussed at past CFSAC meetings. She answered that background work must be done first to define HRSA's involvement, including a set of clear practice guidelines that HRSA would be implementing.

Dr. Klimas noted that the International Association ME/CFS has been discussing developing treatment guidelines for a long time. She asked Dr. Willis-Fillinger how the science community can collaborate with HRSA to move forward on developing such guidelines. Dr. Willis-Fillinger replied that HRSA is not a guideline developing body but that she would discuss the issue with HRSA officials.

Ms. Williams suggested that rather than focusing on formal guidelines, activities center on getting information on treatment options and how well they work. She volunteered to put CFSAC members in touch with officials working with the AHRQ clinical research networks. Dr. Jason suggested that a CFSAC subcommittee be assigned to take advantage of the opportunity being offered by AHRQ and assure that it gets accomplished. The collaboration would meet a great need, is realistically able to be accomplished, and should be a top CFSAC priority, he said.

Dr. Jason then offered a recommendation that he described as a relatively inexpensive first step toward getting some of CFSAC's more expensive goals achieved:

CFSAC unanimously passed the following recommendation: *CFSAC recommends to the Secretary that she recognize the special challenges of ensuring that CFS is included in any efforts to train/educate providers under health reform.*

Dr. Snell commented that once the issue is recognized at the top level of HHS, it starts to move up the priority list elsewhere in the department.

Dr. Jones noted that the thousands of pages of healthcare legislation contain many opportunities for provider education in all health disciplines—not just medicine—particularly for the recruitment of nurses, social workers, and physical therapists. She remarked that there is no better time for CFS to be considered in the context of the broader healthcare arena.

Dr. Jason requested that CFSAC receive feedback on what action is taken by the Secretary as a result of the recommendation. Dr. Jones agreed that the committee should expect feedback, including from *ex officio* members, whose agencies will be involved in healthcare reform. Dr. Snell commented that CFSAC has the opportunity to ask questions and address CFS issues anywhere that is touched by the health reform effort.

Noting that the chart prepared by Dr. Jones of “CFSAC Recommendations Since September 2004” is loosely organized by subcommittee, CFSAC members agreed to use Subcommittee Lunch to prioritize recommendations and provide new members the chance to better familiarize themselves with important issues.

Subcommittees, Present and Future

Mr. Newfield suggested that the continuation of the Patient Care/Quality of Life Subcommittee should be included in CFSAC’s charter considerations. He said that subcommittee members have been discussing whether their time and effort might now be put into more pressing topics. Dr. Jones said that the discussion could move beyond whether or not to continue Patient Care/Quality of Life to encompass a broader discussion reorganizing subcommittees according to which issues should be addressed together.

Dr. Jones announced that attorney Steven Krafchick will be sworn in at the conclusion of Mr. Newfield’s term in July and that Mr. Krafchick has already completed the vetting process.

Dr. Snell suggested breaking into two subcommittees for the purpose of addressing the day’s business—one for a research and one for “non-research” topics, including quality of life. Noting that the Patient Care/Quality of Life Subcommittee was often viewed as the mouthpiece for the patient community, Mr. Newfield emphasized that CFSAC is still interested in those issues and is merely placing them in a broader second subcommittee for one day.

Several CFSAC members commented that patient quality of life has an impact on a broad range of education and research issues. Dr. Jason said that regular subcommittee contact between CFSAC meetings is the only way to have enough time to develop a strategic vision. He noted that the Research Subcommittee has been meeting once a month via conference call facilitated by Dr. Jones’ office.

Strategic vision should be a main function of CFSAC, according to Dr. Miller, including thinking far ahead about what can be accomplished despite current roadblocks. Strategic thinking is looking at the big picture rather than down into the weeds of the details, he continued, and understanding what the Secretary really needs in terms of a recommendation. Dr. Miller said that recommendations are not just wishes; they must be presented in terms of public health outcomes. Dr. Miller concluded that the patient population is looking to CFSAC for leadership in strategic thinking.

Review and Discussion of CFSAC Charter and Bylaws

CFSAC members decided to use the remaining 15 minutes before lunch to begin a discussion of the charter and bylaws.

Dr. Jones gave an overview of the issues:

The charter that is in place at the start of the May meeting differs little from the original charter that created the advisory committee. The proposed draft:

- Amplifies and clarifies the statement of purpose.
- Does not change the authorities.
- Tweaks the functions as per committee discussions in the past.
- Spells out that CFSAC has 11 voting members, with no anticipation of seeking the authority to change that figure. She reminded members that they can always call in subject experts rather than seeking to obligate funds to add a committee member.
- AHRQ has been added as an *ex officio* member. Dr. Jones noted that there have been CFSAC recommendations in the past for adding other agencies.
- Term of service remains four years. The Secretary can appoint a member to fill a vacancy within 90 days, although the current vetting process is taking about 120-140 days.
- Ad hoc subcommittee language is basically the same.
- CFSAC meetings may still occur no more than two times per year. The original Chronic Fatigue Syndrome Coordinating Committee met four times per year for one day. The shift to 2 two-day meetings came when the panel became CFSAC under the Office of Public Health and Science.
- Open meetings are required.
- The CFSAC annual budget is \$130,000.
- There is no change in to whom the committee reports.
- The charter is up for renewal every two years.

Mr. Newfield noted that many in the patient community want to see more than two meetings per year.

Dr. Jason asked that in the interest of time, CFSAC members organize into the two transitional subcommittees before lunch begins. Members aligned themselves into:

Research Subcommittee

Drs. Jason, Glaser, and Hartz + three new members.

- Dr. Jones explained that subcommittees are ad hoc and task-focused. She said that Dr. Jason, whose term ends after the fall meeting, could serve as Research chair until the subcommittee selects someone else.

Subcommittee #2

Dr. Klimas, Mr. Newfield + two new members.

- Dr. Klimas expressed concern that once Mr. Newfield's term expires, the non-research subcommittee would be composed of all women and the more science-oriented research subcommittee would have all male members. Dr. Snell volunteered to bring gender balance to the second subcommittee during the transition. Mr. Newfield suggested that Dr. Klimas remain on the second subcommittee at least temporarily to provide continuity for new members when his term ends.
- Dr. Snell emphasized that a detailed discussion of committee makeup be left for another meeting. He added that experienced members are available to ease new members into the committee culture before their terms expire.
- Dr. Jones explained that subcommittee issues fall under the bylaws.

[Dr. Snell called a break for Subcommittee Lunch.]

Public Comment (on CFSAC charter)

The following section highlights key points made by witnesses who testified during the public comment session. Access to the complete text of witnesses' written testimony is available at: <http://www.hhs.gov/advcomcfs/meetings/presentations/05102010.html>.

John Herd (via phone)

- CFSAC has earned respect from the patient community within the past few years for focusing on challenging issues.
- CFSAC must continue to explore public health agency commitment to good science and effective use of funding, with a focus on:
 - The downward spiral of CFS funding.
 - The funding of only one or two new grants per year.

- The apparent low funding rate for CFS science applications.

Mr. Herd requested that these issues be placed on CFSAC's fall meeting agenda along with a formal report that is due.

Mr. Herd maintained that NIH:

- Has unfortunately chosen to meet the challenge of CFS with “side-stepping, deception through doublespeak, and collaborating systemic malfeasance.”
- Has not stimulated extramural research.
- Has not met its fiduciary responsibilities to people with CFS.

If HHS cannot police itself to meet these responsibilities, Congress should become involved “in ways that we had hoped would not be necessary,” concluded Mr. Herd. His statement was a collaboration with Pat Fero.

Kim McCleary, President and CEO, CFIDS Association of America

- Expressed the desire to go beyond testifying about the charter to address more pressing issues.
- Described many advocates as having a “prevailing sense of defeat” that sitting at the policy table has gotten them nowhere.

Ms. McCleary made the following comments and recommendations on charter revisions:

- The function of CFSAC should be changed to add the development and annual updating of a strategic plan for the conduct and support of CFS research, including budgetary requirements.
- Money is an important focus because Congress is unlikely to appropriate a higher dollar amount than HHS requests.
- CFSAC should develop a cohesive, comprehensive research agenda for HHS that reflects academia, industry, and NGOs.
- CFSAC should add AHRQ and the Centers for Medicare and Medicaid Services (CMS) as *ex officio* members.
- CFSAC should have more interaction with relevant departments, including Defense, Education, Labor, and Veterans Affairs.

Robert Miller (via phone)

- Has been ill for more than 20 years with CFS.
- Thanked Dr. Koh for attending the meeting, noting that it is the first time in more than four years that an HHS Secretary or Assistant Secretary has been in attendance. Expressed hope that Dr. Koh—unlike officials in prior administrations—will follow CFS closely and give the 1-4 million patients the medical concern that they deserve.

- Thanked the HHS Secretary for removing Dr. Reeves from the CFS program, calling it “the first real step our government has taken to validate my illness.”
- Welcomed Dr. Unger and expressed the expectation that the CDC “will aggressively make up for 20 years of lost time.”
- Called on NIH to budget \$100 million for CFS research grants.
- Admonished the FDA for “stonewalling” the approval of Ampligen, which has been in use to treat CFS patients for more than 15 years. Instead, the agency should be coordinating clinical trials, Mr. Miller said.
- Called for two-day CFSAC meetings and extension of member terms when necessary.
- Declared that CFSAC is doing its part, but the only way that the committee can function properly is if it gets a response from the HHS Secretary on vital issues.
- Recommended amending the CFSAC charter to require that the Secretary *will* respond to committee recommendations either directly or through the Assistant Secretary.

Mary Schweitzer (via phone)

In addressing charter renewal there is one basic issue, said Dr. Schweitzer—accountability. Dr. Schweitzer also:

- Called on the US government to accept that it has a massive public health catastrophe on its hands.
- Asserted that the CFSAC mission has made “not one bit of difference in practice” because the health agencies “have paid no attention whatsoever” to what happens at CFSAC meetings. This has created a “stunning disconnect” between what the committee knows and what the CDC and NIH have allowed practitioners and the public to know, according to Dr. Schweitzer, who called on CFSAC to make mediating information a central goal.
- Said that evidence has existed long before the discovery of XMRV that CFS is contagious at some stage of its course, yet the US government let the disease spread unabated for more than 25 years.

Recommended:

1. At least four CFSAC meetings per year until the disease is brought under some measure of control.
2. At least five minutes allotted for the testimony of each member of the public.
3. A continuation of making CFSAC meetings public and making available the records of previous meetings.
4. Allowing audience members to ask questions after *ex officio* members make their presentations.
5. Addressing the problems of children and adolescents.
6. Requiring the HHS Secretary to respond to regular reports sent to her by CFSAC.

7. Reporting CFSAC progress to Sen. Tom Harkin's Committee for Health, Education, Labor, and Pensions. If Federal agencies continue to be unresponsive, there should be a Congressional investigation into why.

Joan Grobstein

- Has had acute onset myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) since 1999. Before her illness, Dr. Grobstein was a neonatologist at Children's Hospital of Philadelphia.
- Expressed disappointment over several aspects of CFSAC meeting logistics: being limited to speaking about charter issues, being given only three minutes to testify, and having only seven public witnesses scheduled to speak.
- Expressed disappointment that Dr. Fred Friedberg, President of the International Association of CFS/ME (IACFS/ME), which represents more than 500 biomedical professionals, did not get to testify.

Charter recommendations:

1. An additional function should be added to establish a consistent definition of ME/CFS and evaluate the likely etiology or etiologies based on that definition. It is surprising that the charter makes no mention of searching for an etiology, since discovering and verifying it is essential for all other CFSAC functions. The Canadian Consensus definition of CFS is accurate and consistent and should be included in the charter, she said.
2. The charter should require real time and recorded video casts of CFSAC meetings as a necessary accommodation of ME/CFS patients.
3. The charter should require CFSAC to meet four times a year for two days and conduct a complete status report of current and past recommendations at each meeting.

Nancy McGrory Richardson, Education and Outreach Director, Hemispherx

- FDA has issued a complete response letter regarding Hemispherx' new drug application. The agency recommends at least one additional clinical study to show convincing effect and confirm the safety of the target population.
- Hemispherx has instituted a new clinical study protocol to retrospectively monitor the blood of patients enrolled in its 516 study to identify target subsets of patients who are most likely to benefit from Ampligen treatment. The study will be conducted in conjunction with WPI and will monitor patients for evidence of XMRV. When the study is complete this summer, the data will be used along with the FDA recommendations to design the next clinical study for Ampligen.
- Hemispherx has awarded IACFS a grant to conduct a clinical guidelines workshop this month.
- Hemispherx has made a significant investment in a biological manufacturing facility in New Jersey to produce Ampligen.

Annette Whittemore

- Pointed out that CFS patients lack a medical specialty to rely on for care. Confusion continues over the true nature and severity of this disease, which results in the sick being turned away without proper medical care as well as the wide dissemination of misinformation.
- Expressed deep concern that NIH has not established funding to directly support outside researchers who wish to continue important XMRV and ME/CFS studies.
- Called for a recommendation to the HHS Secretary that NIH make ME/CFS a research priority by dedicating research dollars that match the number of individuals impacted by CFS. Called on NIH to do for CFS what it did for multiple sclerosis and lupus.
- Called for funding for translational medical research centers of excellence.
- Called for CFSAC charter renewal to be based on evidence of the achievement of goals and implementation of recommendations.

Ms. Whittemore concluded that while an open dialog with the HHS Secretary is important, so is acting upon CFSAC recommendations as quickly as possible.

Dr. Snell noted that CFSAC is looking into extending the time for public comment at future meetings from three minutes per witness to five minutes per witness. He then extended the public comment period for another 10 minutes to accommodate two more witnesses.

Dr. Fred Friedberg, President, IACFS/ME

Endorsed the CSFAC charter because:

- The committee is the sole government-sponsored group to provide a national forum for a scientific and public policy discussion related to CFS.
- The committee is uniquely suited to serve as an independent voice for the important concerns of the medical and research communities, including a definition of the illness. The 2003 Canadian Case definition offers substantive improvements over currently used definitions because it better identifies CFS symptoms and makes a clearer distinction between psychological and physical illness.

Dr. Friedberg proposed that:

- CFSAC open a regular session for research presentations and an ongoing discussion focused on the Canadian criteria.
- CFSAC restore its two-day schedule to allow for scientific presentations, public testimony, and useful interaction among committee members.

Pat Sonnett

Addressed four points about the CFSAC charter:

1. Supported renewal of the charter.
2. Called for a charter amendment directing CFSAC to hold two-day meetings four times per year rather than twice a year.
3. Called for the charter to include a provision for the video webcasting of CFSAC meetings. If webcasting is not in the charter, it could be removed at any time.
4. Amend the charter to include status reports at least twice a year on CFSAC recommendations to the HHS Secretary so the patient community can track their progress.

Review and Discussion of CFSAC Charter and Bylaws

CFSAC members reopened their discussion of the committee charter and bylaws. **Dr. Jones** explained the importance of approving a charter by the end of the current meeting because the finalization process takes about 90 days and the current charter expires on September 5, 2010, more than a month before the next CFSAC meeting.

To ensure that a charter is approved by the end of the meeting, Dr. Jason moved that CFSAC approve the draft charter dated April 30, 2010 with the provision that it will be amended. CFSAC unanimously approved the amendment.

Adding CMS as Ex Officio

Dr. Jason commented that both written and oral public testimony presented many well-articulated ideas for charter amendments and offered one that had been proposed by **Ms. McCleary**:

CFSAC unanimously approved the following amendment: Amend the charter to add the Centers for Medicare and Medicaid Services (CMS) as an ex officio member and add liaison representatives from the Departments of Defense, Education, Labor, and Veterans Affairs.

Dr. Jones noted that from a health reform perspective, “CMS has its hand on the purse.” **Ms. Williams** said that in addition to being the payer for Medicaid and Medicare in the states, CMS is also involved in quality improvement and is integral to CFSAC activities.

Public Testimony

Dr. Jason offered another amendment:

The equivalent of one hour of each CFSAC meeting day will be dedicated to receive testimony from public witnesses delivered either in person, by telephone, or by video. The period of time allocated to each witness will be not less than five minutes.

Witnesses can use their allocated time to read a prepared statement, to offer comments on committee reports or discussion, or to ask questions of the committee.

In discussing the amendment, CFSAC members made the following points:

- Logistical complications may result when witnesses use their time to ask complex questions of committee members that cannot be answered in the five-minute time slot. **Dr. Marshall** proposed creating a separate amendment that would allow the public to submit written questions beforehand to be answered at meetings during a designated time slot. Dr. Jason accepted the friendly amendment.
- In the past, when CFSAC was still a coordinating committee, members had more flexibility for exchanges with the public. These exchanges helped to educate committee members.
- Some CFSAC members favored automatically giving long-standing CFS organizations the time to ask questions. Other members maintained that such an arrangement would stymie a broader variety of viewpoints.
- Members discussed how the order of speakers would be determined. Dr. Jones said that with the exception of the current one-day meeting, CFSAC has been able to accommodate requests for public comment slots. Because time was limited for this meeting, her staff drew names.
- Dr. Jones explained that if the procedures being discussed (one-hour minimum for public comment, drawing slots, etc.) are codified in the charter, they will have to be followed every meeting as part of CFSAC's obligation under the Federal Advisory Committee Act. The meeting would have to provide one hour of public comment, for example, even if there were only enough witnesses to fill 30 minutes. As a result of this discussion, Dr. Jason's proposal was amended to give public witnesses "the equivalent of up to one hour" of each CFSAC meeting day.
- Committee members debated public comments and question/answer sessions should be scheduled at the same time. Scheduling could be easily upset by complex or prolonged answers. Several members suggested that question/answer sessions should be scheduled separately from public testimony. Dr. Jason agreed to remove the question/answer portion from his proposal.
- At Dr. Jones' suggestion, CFSAC made the amendment apply to the committee bylaws rather than place it in the charter where it would have to be followed for two years.
- Dr. Jones suggested that the committee also address webcasting in the bylaws so that changes can be made to accommodate technological advancements. She described the bylaws as the CFSAC "standard operating procedures manual" of how the committee implements the charter. Although bylaws are more detailed, they can be changed by the committee on a moment's notice.
- Dr. Jones noted that this is the first time that CFSAC has had bylaws and said that they will be a great help to future DFOs and *ex officio* members. Dr. Jones added that the General Services Administration strongly recommends that advisory committees have bylaws.

- Committee members decided that written questions from the public should be dispersed by the CFSAC chair and that questions may go to *ex officio* members. **Dr. Snell** said that it remains to be worked out exactly how the question/answer period will be fit into the meeting schedule.

CFSAC unanimously passed the following amendment to its bylaws: *Up to one hour of each meeting day will be dedicated to receive testimony from public witnesses delivered either in person, by telephone, or by video. The period of time allocated to each witness shall be not less than five minutes. Witnesses can use their allocated time to read a prepared statement, or offer comments on committee reports or discussion.*

CFSAC members directed Dr. Jones to edit the draft bylaws to bring statements about public testimony in line with the just-passed amendment.

Public Question/Answer Session

CFSAC next turned to Dr. Jason's bylaw motion to:

- Allocate one hour of each CFSAC meeting to questions submitted by individuals to the Chair.
- Distributed questions at the Chair's discretion to the appropriate voting or *ex officio* members.
- Allocate five minutes per witness testimony. (?)

CFSAC members discussed the pros and cons of handing questions to the Chair during the meeting vs. submitting them ahead of time. Dr. Jones said that CFSAC must consult its advisory committee lawyers for advice on this subject.

Dr. Jason tabled his motion pending legal advice. He said that some of the most riveting moments at committee meetings have been when someone from the audience has come to the table for an unplanned dialog with members. Dr. Jason urged that CFSAC have the flexibility to conduct such dialogs.

Dr. Hanna expressed concern about *ex officio* members being asked to give information that they have not cleared with their agencies. Anyone can write to an agency and get answers, but there are procedures and guidelines that must be followed, she said. She urged Dr. Jones to discuss this issue with committee counsel. Dr. Jones agreed, noting that a dialog with the public is not the same as a witness serving as an expert to an advisory committee. She emphasized that CFSAC is not discouraging a dialog, merely checking on the rules for fairness and transparency. Dr. Snell said that CFSAC will more fully discuss the issue when members have more information.

Etiology and Biomarkers

CFSAC members unanimously approved a charter amendment to be added to the Function section on page one of the April 30, 2010 draft to add the words “etiologies” and “biomarkers” to read: “...(1) the current state of knowledge and research about the epidemiology, etiologies, biomarkers, and risk factors relating to chronic fatigue syndrome and identifying potential opportunities in these areas.”

Meetings

CFSAC members unanimously approved a charter amendment to be added to the Meetings section on page two of the April 30, 2010 draft so that the third sentence in the paragraph reads: Development of the meeting agenda will be done in collaboration with the Committee Chair and the Subcommittee Chairs or their designee.”

Actions on Recommendations

CFSAC members discussed the issues associated with a recommendation by Dr. Jason: Following each CFSAC meeting the Chair of the CFSAC will meet with the Assistant Secretary of Health to review recommendations. There will be a mechanism established so that each recommendation made to the Secretary will have a specific response announced to the CFSAC members and the public.

Issues discussed included:

- The Assistant Secretary has 11 advisory committees reporting directly to him and may realistically be unable to meet with the CFSAC Chair as described in the recommendation.
- Dr. Jones reminded the committee that CFSAC cannot control how the Secretary responds to recommendations, the charter does not address HHS processes, and the proposed amendment would likely be struck down by counsel. The amendment could be placed in the bylaws, she said, as something the committee would strive to do—have a conference call after meetings to discuss recommendations. But CFSAC cannot guarantee the level of commitment from the Secretary or Assistant Secretary.
- Dr. Jones suggested that all recommendations be transmitted from and signed by Dr. Snell as CFSAC Chair rather than by her. Dr. Jones observed that recommendations signed by the Chair seem to carry more weight.
- Dr. Jones noted that delayed action on some recommendations may have to do with budgetary timing rather than inaction. A recommendation may arrive with the Secretary when all funds have already been allocated for the fiscal year.
- **Dr. Klimas** suggested that the charter amendment be passed instead as a bylaw and Dr. Jason accepted the friendly amendment.
- Because **Dr. Koh** has already committed to more interaction with CFSAC, Dr. Snell proposed “softening” the sentence to say that “every effort should be made” to meet. Dr. Jason accepted the friendly amendment.

CFSAC members unanimously approved the following amendment to its bylaws: *Following each CFSAC meeting, every effort should be made by the Chair to meet with the Assistant Secretary of Health to review recommendations. There will be a mechanism established so that each recommendation made to the Secretary will have a specific response announced to the CFSAC members and the public.*

Strategic Plan

CFSAC members discussed Dr. Jason's next amendment:

The CFSAC will develop a strategic plan for CFS research. This plan will be submitted to Congress each year. The committee will monitor Federal activities with respect to CFS and make recommendations to the Secretary of HHS regarding any appropriate changes to such activities based on the status of the field.

Discussion points included:

- CFSAC advises the Secretary and has nothing to do with Congress.
- Dr. Jones commented that although advisory committees have historically gotten engaged in Departmental strategic planning processes, she is not aware of any committees that have been specifically charged with strategic planning. She added that many advisory committees are interacting with overall research planning and that NIH and CDC have strategic planning underway. She advised articulating a more concrete role for CFSAC.
- Ms. McCleary was called to the witness table to clarify her position on CFSAC strategic planning. She said that she took her language straight out of the objectives and scope of activity for the charter of the Interagency Autism Coordinating Committee. She acknowledged that there is a difference between an interagency committee as opposed to a single department advisory committee. The idea, she said, is to avoid many single recommendations that do not fit into a greater framework.
- A strategic plan could be aimed at the HHS Secretary as opposed to Congress.
- CFSAC members debated formulating the plan in collaboration with agencies outside the committee.
- Dr. Jones suggested focusing over the next year on getting the information needed for a strategic plan. She noted, however, that if this is made part of the charter, CFSAC is locked into formulating a strategic plan, possibly at the expense of other topics. She said that the committee has room within the functional language of the charter to focus on a strategic plan.
- The new liaison departments could participate in developing a strategic look at the needs and gaps in the CFS field.
- The Assistant Secretary of Health could write a letter to his counterparts at those departments inviting them to join in.

Recognizing that strategic planning can occur without a formal statement in the CFSAC charter, Dr. Jason tabled his motion.

Quality of Life

CFSAC members unanimously approved a charter amendment to be added to the Function section on page one of the April 30, 2010 draft to read: “...and (4) improve the quality of life for CFS patients.”

Meeting Length

Dr. Jason introduced the idea of a three-day CFSAC meeting—possibly in the fall—in which the first day is devoted to thinking about science and the issues in the field.

- Dr. Klimas suggested amending the charter to read “at least 2 two-day meetings” to preserve scheduling flexibility.
- Dr. Jones said that each meeting costs \$65,000 including staff and video casting. She said that the committee is “highly unlikely” to get more funding for 2011.
- **Dr. Miller** noted that CDC and NIH contribute funding to the CFSAC budget. He said that perhaps the other *ex officio* agencies could also begin contributing.
- Dr. Jones said that schedules vary among the other 150 advisory committees and include teleconferencing, webinars, and site visits.
- Dr. Jason proposed inserting into the bylaws that CFSAC members do thoughtful preparation before meetings on issues that can then be debated at the meeting.
- **Dr. Houghton** expressed surprise that the CFSAC budget is so constrained that it cannot react to new developments such as the XMRV research. He asked whether it is possible, given the excitement generated by WPI, to get more funds for meetings.
- Dr. Jones suggested that the issue is more appropriate as a recommendation rather than as part of the charter or bylaws.
- **Dr. Marshall** asked the committee to explore technology options such as webinars to allow more frequent meetings, especially for the “nitty gritty and elbow grease work” that needs to be done. He noted that the research subcommittee is already meeting once a month.
- Dr. Jones said that her staff could be directed to explore webinar and report back for the fall meeting. She estimated that a webinar CFSAC meeting would cost about \$10,000.
- Dr. Marshall proposed a recommendation to “Actively explore the value and need for a webinar extra meeting in the 2011 year for the entire committee.” The motion was tabled pending action on the charter amendment:

CFSAC members unanimously approved a charter amendment to be added to the first sentence of Section IV: Meeting Procedures so that it reads: “Meetings of the full committee shall be held no less than twice a year and for no less than four days...”

October 2009 Minutes

CFSAC members unanimously approved the minutes from the October 29-30, 2009 meeting.

Diagnostic and Treatment Demonstration Project

Dr. Klimas proposed a recommendation based on Subcommittee #2's discussion of developing evidence-based guidelines for treating CFS. The panel discussed that:

1. AHRQ, HRSA, and CMS have an interest in cost-effective, efficient, effective healthcare and the potential financial resources to fund pilot projects.
2. AHRQ and HRSA have public and private venues where demonstration projects can take place.

The subcommittee made the following recommendation:

The Education and Quality of Life Subcommittee [Subcommittee #2] recommends that CMS/AHRQ/HRSA develop a private and public demonstration project to put into place diagnostic and treatment paradigms that would result in effective and efficient assessment and therapeutic care and result in improved health outcomes and better value of invested healthcare dollars.

- Dr. Klimas explained that the idea would be to monitor diagnostic and treatment paradigms to see whether they make a difference in outcomes of patient health. She gave the example of a healthcare system like Kaiser using survey instruments to capture a fatigue population. That survey population would be given a set of instruments that would capture various aspects such as sleep autonomies. Diagnostics would then ensue and based on those, patients would receive appropriate treatments. The project would streamline the assessment and treatment processes and determine whether patients did better and whether money was saved.
- **Ms. Williams** said that either HRSA or AHRQ could undertake such a project, most likely working with existing systems that have an academic partner.
- Dr. Jason asked if there are funding mechanisms available for such a project. Ms Williams replied that she could not speak to the funding.
- **Dr. Cook** said that the VA medical centers conduct a similar activity with chronic pain in their health services research. Centers conduct comparative effectiveness research within their chronic pain working groups to see whether or not their own chronic pain management style results in better outcomes than the standard of care style.

- Ms. Williams explained that AHRQ has two standing programs that are research networks. One is a primary research network and the other is an integrated research network. AHRQ selects who is going to be part of the network, then puts out task orders for bidding.
- Dr. Jones emphasized that under health reform there is significant interest in comparative effectiveness and health services research, particularly demonstration projects that show new ways of tackling complex problems.
- Dr. Willis-Fillinger said that HRSA is searching for organizations that would like to work with the agency on comparative effectiveness research. She said that these will more likely be organizations that HRSA already funds and those that have experience with collaborative learning and quality improvement.
- Dr. Snell summarized the recommendation's premise: The current treatment model is costing a lot more than it has to and it is not effective.
- Committee members debated whether to call the activity a "research" project or a "demonstration" project. Dr. Jones maintained that "demonstration" would be more accepted in the current health environment than the narrower term "research."

CFSAC members unanimously approved the following recommendation to the HHS Secretary: CFSAC recommends that CMS/AHRQ/HRSA develop a private and/or public demonstration project to put into place diagnostic and treatment paradigms that would result in effective and efficient assessment and therapeutic care and result in improved health outcomes and better value of invested healthcare dollars.

Webinar-Based CFSAC Meeting

CFSAC members unanimously approved the following recommendation: CFSAC recommends to the HHS Secretary that she ask Dr. Jones' office to actively explore the feasibility of a webinar-based third CFSAC meeting in 2011 based upon the value of carrying on a meeting in that format.

- Dr. Marshall said that he offered the recommendation in hopes of providing a rational reason for the HHS Secretary to fund the \$10,000 needed for the webinar. Dr. Marshall noted the number of public comments calling for more frequent CFSAC meetings. The financial and planning logistics inhibit more face-to-face gatherings, but if CFSAC can show that a third meeting via webinar can add value to the committee's function, it is a means of addressing public comments in the face of a tight budget.

- In answer to using technology such as Skype, Dr. Jones replied that CFSAC must adhere to Federal data systems security, public access rules, etc. She said that Skype-type technologies would be appropriate for subcommittee meetings.

Because time ran out for CFSAC members to prioritize the committee's previous recommendations, Dr. Snell asked each member to provide that feedback, predicting that "we won't be far apart" in ranking the most important items.

Reclassification of CFS

Dr. Klimas urged CFSAC to consider past recommendation 3.a.9.04, to encourage the classification of CFS as a "Nervous System Disease" as worded in the ICD-b G93.3, the World Health Organization's disease classification system. She explained that CFS is in danger of being reclassified under the psychiatric coding this summer, an action that has major implications for CFS patients.

CFSAC members unanimously approved the following recommendation: *CFSAC strongly rejects the proposal to classify CFS as a psychiatric condition in the ICD 10.*

In closing...

- Dr. Snell directed CFSAC members to choose one or two top priorities from past recommendations in each of three categories—"free, expensive, and mid-level."
- Dr. Snell commended Jason Newfield for his exceptional service to CFSAC over the last four years.
- Mr. Newfield said that he is humbled and inspired to have been part of the group and has been inspired by the patient community as well. Dr. Jones thanked him for his dedication and commitment.

Adjournment