DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CENTER FOR COMPLEMENTARY
AND ALTERNATIVE MEDICINE

NATIONAL ADVISORY COUNCIL FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE
MINUTES OF THE FORTY-SEVENTH MEETING
October 12, 2012

NACCAM Members Present

Dr. Brian Berman, Baltimore, MD
Dr. Adam Burke, San Francisco, CA
Dr. Daniel Cherkin, Seattle, WA
Dr. Steven DeKosky, Charlottesville, VA
Dr. Stephen Ezeji-Okoye, Palo Alto, CA
Dr. Susan Folkman, San Francisco, CA
Dr. Jane Guiltinan, Seattle, WA
Dr. Scott Haldeman, Santa Ana, CA
Dr. Frances Henderson, Jackson, MS
Dr. David Kingston, Blacksburg, VA
Dr. John Licciardone, Fort Worth, TX
Dr. Philippa Marrack, Denver, CO[1]
Dr. Lloyd Michener, Durham, NC
Dr. Linda Powell, Chicago, IL
Dr. Katherine Shear, New York, NY
Dr. Xiaoming Tian, Bethesda, MD

[1] Telephone

SPEAKERS

Dr. Michael Barry, Boston, MA
Mr. John Burklow, Bethesda, MD

NACCAM Members Not Present

Dr. Gary Curhan, Boston, MA
Dr. Richard Niemtzow, Clinton, MD

NIH Staff Present

Jiaxu Chen, NCI, NIH
Ned Curhan, OLPA, OD, NIH
Mary Gracia, NIH

Johnny Ivanovich, OHR, OD, NIH
Denise Peterson, OHR, NIH
Barbara Sorkin, ODS, NIH
Dan Xi, OCCAM, NCI, NIH

Members of the Public

Maguerite Clarkson
Steven Dentali
Cathleen Kearns
Judith Mun
Herb Simmens

I. Closed Session

The first portion of the forty-seventh meeting of the National Advisory Council for Complementary and Alternative Medicine (NACCAM) was closed to the public, in accordance with the provisions set forth in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

A total of 249 applications were assigned to NCCAM. Of these, 139 were reviewed by NCCAM, 110 by Center for Scientific Review. Applications that were noncompetitive, not discussed, or were not recommended for further consideration by the scientific review groups were not considered by Council.

Council agreed with staff recommendations on 103 applications, agreed with IRG recommendation on 1 application, requesting $36,469,907 in total costs.

II. Open Session—Call to Order

The open session convened at 10:45 a.m. Dr. Martin Goldrosen, NACCAM Executive Secretary, called the meeting to order.

The minutes of the June 1, 2012, in-person NACCAM meeting, and the August 27, 2012 NACCAM teleconference were approved unanimously.

Dr. Goldrosen recognized and thanked Willer "Dean" Batten, who will be retiring in December 2012 after 42 years at the National Institutes of Health (NIH). Ms. Batten has helped organize the NACCAM meetings since their inception.

III. NCCAM Director's Report

NCCAM Director Dr. Josephine Briggs recognized four retiring Council members: Drs. Adam Burke, Katherine Shear, and Xiaoming Tian, who have completed their terms of service, and Dr. Janet Kahn, who has accepted a position on another federal advisory council.

Dr. Christopher P. Austin has been appointed Director of the National Center for Advancing Translational Sciences (NCATS). A search will now begin for a permanent director for NCATS' Division of Clinical Innovation to replace Dr. Briggs, who has been serving as acting director of that division in addition to her responsibilities at NCCAM.

Dr. Catherine Bushnell joined NCCAM 3 months ago as the Scientific Director of the Division of Intramural Research. She will present a report to Council at the next meeting.

The Federal Government is currently operating under a 6-month continuing resolution. As during previous continuing resolutions, NCCAM will operate with a set of conservative budget assumptions in establishing interim funding policy.

Dr. Briggs and Council members discussed the budget mechanism table. At any one time, NCCAM funds approximately 350 projects, both new and continuing. She pointed out that most of NCCAM's research funds are committed to continuing projects. For example, in fiscal year 2012, $18 million of NCCAM's $92 million allocation for extramural research grants was available for new awards.

Dr. Briggs recently spoke at a Congressional Caucus meeting on alternative solutions to the prescription drug epidemic, and met with Congressman Tim Ryan to discuss NCCAM-funded research on mindfulness meditation. An important meeting of the data safety and monitoring board for the NCCAM-funded clinical trial of creatine in Huntington's disease took place in September. NCCAM co-sponsored an NIH workshop on chronic overlapping pain conditions in August. Other recent activities include a yoga blogger roundtable, a *Wall Street Journal* briefing about NCCAM's focus on treating pain and its new intramural research program, and continuing monthly Twitter chats.

Dr. David Kingston of Virginia Tech (Virginia Polytechnic Institute and State University) will present NCCAM's Distinguished Lecture in December. The Office of Dietary Supplements and NCCAM have invited a distinguished panel to evaluate the Botanical Research Centers Program before its planned recompetition in 2014. NCCAM is playing a significant role in the Health Care Systems Research Collaboratory, in which NIH will partner with health care systems to conduct clinical research in the settings where patients already receive their care.

Highlights of recently published NCCAM-sponsored research include:

- An individual patient data meta-analysis on acupuncture for chronic pain by Dr. Andrew Vickers of Columbia University and colleagues, which showed a sizeable benefit of acupuncture compared with no-acupuncture controls and a more modest difference between acupuncture and sham acupuncture. This publication received substantial news media attention.

- A study showing that subliminal cues can activate placebo and nocebo responses.

- The results of a carefully conducted trial of oral silymarin on liver disease in patients with chronic hepatitis C, which found no beneficial effects.

Dr. Briggs concluded her presentation by drawing members' attention to *Escape Fire*, a new documentary film on the American health care system, which includes input from several champions of integrative approaches to health care.

IV. Task Force on Research Standards for Low-Back Pain Update

NCCAM Program Officer Dr. Partap Khalsa updated Council on the efforts of a task force of the NIH Pain Consortium to develop research standards for low-back pain. The task force is developing a draft set of research standards for clinical studies, which includes an operational definition of chronic low-back pain, a minimal dataset of demographic and bio-psychosocial factors, and recommendations for standardized outcome metrics. Research diagnostic criteria may also be included, but such criteria are most useful for conditions that have identifiable etiologies, and most cases of low-back pain do not. The National Institute of Neurological Disorders and Stroke core data elements are being used as an organizing principle.

The task force has met twice, in March and October 2012, and plans one more meeting to finalize the draft standards before submitting them to a large stakeholder meeting. Key challenges for the task force are that:

- Back pain is a symptom rather than a disease
- Multiple professions and subspecialties provide a wide range of diagnostic and treatment approaches
- Defining "chronic" is problematic because of the highly variable and often relapsing-remitting pattern seen in many patients.

Discussion. Dr. Briggs and Council members commented on the difficulty of this undertaking. Members expressed the view that patient-reported outcomes should be considered as important as physical measures. Dr. Khalsa indicated that the task force is in fundamental agreement. In response to members' questions, Dr. Khalsa clarified that the task force had concluded that imaging is of little value in most cases of chronic low-back pain, but it is sometimes needed for diagnosis of certain well-identified specific etiologies. He also explained that the task force's charge is focused on standards for research, not treatment in clinical practice, and that the task force is addressing the challenge of defining chronicity. Dr. Briggs noted that the task force's work is particularly challenging because it involves experts from many disciplines, making achievement of consensus difficult.

V. NIH Communications: Making the Connection

John Burklow, NIH Associate Director for Communications and Public Liaison, briefed Council on how NIH is positioning itself in public discourse. Currently, too few people understand what NIH is, what it does, and how it makes a difference in Americans' lives. Only 9 percent of respondents to a national poll mentioned NIH in response to the question "Do you know of any institutions, companies, or organizations where medical or health research is conducted?" Many

members of Congress have urged NIH to make its role better known so that their constituents will understand the need for NIH funding.

Improved communication of NIH's role is also needed because of the current climate in several areas, including:

- **The budget climate.** Tight economic times demand a strong case for the value of NIH research.

- **The communications climate.** The fragmented media world requires a cohesive NIH identity.

- **The community climate.** Diverse stakeholders have competing interests and need a common goal.

NIH faces the challenge of communicating the value of its research with maximum impact. Making NIH communications more unified is one important step in addressing this challenge. Currently, most communications come from individual institutes and centers (ICs), and people may not realize that these ICs are part of NIH. Putting NIH forward when communicating with the public, but not to the exclusion of the ICs, is a top priority.

The NIH communications office is moving toward the development of a common visual identity, including a strong common logo that would tie the individual ICs to NIH as a whole. Efforts are also being made to put together a communications toolkit and other resources for NIH staff. NIH is asking stakeholders and grantee institutions to mention NIH in press releases and interviews and is strengthening stakeholder relations. NIH leaders and staff are being encouraged to communicate in whatever ways are comfortable for them; Mr. Burklow gave as an example the appearance on *The Colbert Report* of NIH Director Dr. Francis Collins, who talked about obesity and NIH's role in the development of the HBO documentary series *The Weight of the Nation.*

Mr. Burklow showed highlights from "NIH Day," held as part of the Milken Institute-sponsored Celebration of Science in September. This event showcased the impact of NIH research on people's lives. The challenge now, Mr. Burklow said, is to continue the momentum from this event and keep telling NIH's story.

Discussion. Council members commented that it is more difficult to help people understand the impact of basic science than it is for clinical science. Mr. Burklow agreed, noting the importance of helping people understand how basic research eventually contributes to improved medical treatments. Dr. Briggs said that NCCAM is already making an effort to identify itself as the part of NIH that studies complementary health practices and that NCCAM is looking forward to building a logo and other aspects of branding with NIH. Mr. Burklow said that NCCAM is one of the few ICs that explicitly connects itself to NIH on its home page. He also complimented NCCAM for its active involvement in social media.

VI. Complementary and Alternative Medicine for Urological Symptoms (CAMUS) Study

Dr. Michael Barry of Harvard Medical School presented a summary of a recently completed NCCAM-supported, multicenter, double-blind trial of increasing doses of saw palmetto extract for lower urinary tract symptoms in men, called the Complementary and Alternative Medicine for Urological Symptoms (CAMUS) study.

The CAMUS study was initially designed as a 3,300-participant, 4-armed trial to evaluate the effects of saw palmetto extract, a second plant extract, an alpha-blocker (as a positive control), and placebo on long-term prevention of progression of urinary tract symptoms associated with benign prostatic hyperplasia. However, the design was modified after a 2006 randomized trial of saw palmetto found no significant benefit over placebo.

The final study objective was to conduct a randomized, placebo-controlled, double-blind trial to determine whether a standard dose of saw palmetto extract, increased to a double and then a triple dose over 72 weeks, would improve urinary tract symptoms associated with prostate enlargement. The trial took place at 11 sites in North America between 2008 and 2010, and 369 participants were randomized.

Blinding participants and investigators to the participants' treatment assignments was a challenge because of the distinctive odor of saw palmetto. The researchers decided to individually package the study medications in blister packs to conceal the odor. At the end of the study, there was no significant difference between patient groups in their ability to correctly identify the treatment they were receiving, which indicated that blinding was successful.

After 72 weeks, saw palmetto produced no better results than placebo in terms of the primary outcome (scores on the American Urological Association Symptom Index) or any secondary outcome. Approximately half of all men taking either saw palmetto or placebo had a meaningful improvement in their symptoms. Men taking saw palmetto did not have a greater number of total or serious adverse events or a greater number of abnormal laboratory test results than those taking placebo. The principal findings of the trial were published in the *Journal of the American Medical Association*.

Dr. Barry explained that the standard, efficacy-oriented interpretation of the results of this trial is that increasing doses of saw palmetto extract did not reduce lower urinary tract symptoms compared with placebo. However, an alternate, effectiveness-oriented interpretation is that about half of men taking saw palmetto had an improvement in their symptoms, with virtually no side effects. Views differ on which interpretation of the results is more appropriate, especially for communication with patients.

Discussion. Dr. Briggs noted that although the results of this study did not demonstrate evidence of benefit, they are important because of the rigor of the trial that produced them. She reminded the Council of evidence that both "positive" and "negative" studies supported by NCCAM have had an impact on use by the public and have received extensive media coverage. She also noted evidence that many of the highest-impact NHLBI papers in the scientific literature reported "negative" results.

Council members congratulated Dr. Barry on this impressive, carefully performed study. In response to members' questions, Dr. Barry explained that symptomatic improvement was seen in half of the participants in the placebo group as well as in half of those taking saw palmetto; that he and his colleagues performed one-tailed statistical tests because they felt that from a clinical perspective, it would not matter whether saw palmetto was the same as or worse than placebo; and that the results of this study will be incorporated into official guidelines for the treatment of benign prostatic hypertrophy.

VII. Update on Collaboration Between NCCAM and the U.S. Military

NCCAM Program Officer Dr. Kristen Huntley reported on progress made on initiatives to stimulate research on the use of complementary approaches to pain and symptom management in military and veteran populations. Council approved this concept in June 2012.

In the first phase of this effort, NCCAM published a funding opportunity announcement (FOA), soliciting applications for small administrative supplements to currently funded NCCAM grants to plan collaborative activities with Department of Defense or Department of Veterans Affairs researchers or clinicians. NCCAM funded seven supplements: two on planning, resource sharing, or secondary data analysis; two on mindfulness-based stress reduction; and one each on tai chi, spinal manipulative therapy, and massage.

The second phase will involve issuance of an FOA to encourage NCCAM investigators to collaborate and further expand funded research on the use of complementary approaches for symptom management in military and veteran populations. The FOA should be released in November.

The third phase involves working with partner ICs to develop a trans-NIH FOA to encourage research on pain management in military and veteran populations. This concept was presented to the NIH Pain Consortium in July, and two NIH ICs have expressed interest. The FOA will be released in early 2013.

Discussion. In response to members' questions, Dr. Huntley explained that researchers need not have been involved in the first phase of this project to be eligible to participate in the second phase. The second phase will allow investigators in areas of interest specified in the FOA to submit applications.

VIII. Update on Herb/Drug Interactions

NCCAM Program Officer Dr. Craig Hopp presented an update on the progress that has been made on NCCAM's herb/drug interactions project. Council approved this concept in June 2012.

As background, Dr. Hopp noted that the journal *Planta Medica* devoted its September 2012 issue entirely to publications on herb/drug interactions, several of which were authored by experts who participated in NCCAM's March 2012 interactions workshop. Dr. Hopp noted that in addition to potentially harmful interactions, NCCAM's interests also include potentially beneficial interactions such as those highlighted in recent news coverage of interactions between cancer

drugs and grapefruit juice. The news media presented these interactions as desirable because grapefruit juice slows the metabolism of the costly drugs, thereby allowing smaller doses to be used.

The first phase of NCCAM's herb/drug interaction project involves establishing criteria for priority setting and generation of an interaction testing matrix. To begin this process, NCCAM has assembled and will work with an expert panel which will review the findings of an extensive literature search to identify reported interactions and the type of evidence supporting them. The panel will have an in-person meeting in the spring of 2013. Subsequent phases will involve systematic *in vitro* and where necessary *in vivo* research focused first on those herb/drug interactions for which additional information is most urgently needed, and disseminating findings of this research to the scientific community and the public.

Discussion. Dr. Daniel Cherkin asked whether data from electronic health records could be used to identify instances of herb/drug interactions. Dr. Briggs replied that this would be difficult because supplement use is imperfectly reflected in health care records. However, some subsets of records may have sufficient supplement information to be useful for this purpose. Dr. Tian commented that in China the concept of beneficial interactions between herbs and drugs is well accepted. Dr. Briggs reminded the Council that the data on most herb/drug interactions are quite soft. In response to questions about case studies, Dr. Hopp explained that the experts at the March workshop viewed case reports with suspicion because of difficulties in determining which products an individual may have been taking, and in confirming the actual content of an implicated herbal product.

IX. Public Comment and Adjournment

Mr. Herb Simmons of the District Wellness Group told the Council that he had been diagnosed with lung cancer more than 20 years ago and was treated at the time with the Gonzalez regimen. He questioned the findings of the 2009 NIH-funded clinical trial of this regimen, which found it to be inferior to chemotherapy in patients with pancreatic cancer. He urged Council members to read Dr. Gonzalez's book *What Went Wrong: The Truth Behind the Clinical Trial of the Enzyme Treatment of Cancer,* which criticizes the methodology of the trial, and to consider conducting further studies of the Gonzalez regimen.

No other public comments were offered.

The meeting adjourned at 3:25 p.m.

We hereby certify that, to the best of our knowledge, the foregoing minutes are accurate and complete.

Martin Goldrosen, Ph.D.
Executive Secretary
National Advisory Council for

Josephine Briggs, M.D.
Chairperson
National Advisory Council for

Complementary and Alternative Medicine