

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 FORTIETH MEETING "
September 3, 2010 "

NACCAM Members Present

*Dr. Lori Alvord, Hanover, NH
Dr. Stephen Barnes, Birmingham, AL
Dr. Timothy Birdsall, Goodyear, AZ
Dr. Gert Bronfort, Bloomington, MN
Dr. Adam Burke, San Francisco, CA
Dr. Lupo Carlota, Memphis, TN
Dr. Sheldon Cohen, Pittsburgh, PA
Dr. Gary Curhan, Boston, MA
Dr. Steven DeKosky, Charlottesville, VA
Dr. Stephen Ezeji-Okoye, Palo Alto, CA
Dr. Susan Folkman, San Francisco, CA
Dr. Janet Kahn, Burlington, VT
Dr. Shin Lin, Irvine, CA
Dr. Richard Niemtow, Clinton, MD
*Dr. Katherine Shear, New York, NY
*Dr. Herman Taylor, Jackson, MS

*Teleconference

NACCAM Members Not Present

Dr. Boyd Bowden, Columbus, OH
Dr. Margery Gass, Mayfield Heights, OH
Dr. Xiaoming Tian, Bethesda, MD

NIH Staff Present

Mirian Alkliddar, OCCAM, NCI
Andrea Baruchin, OD, AUX, FNIH
Stephanie Bonhomme, OD, OHR, NIHTC
Liberty Bost, OD, OHR, NIHTC
Andrea Collins, CMO, NCI
Edward Culhan, OD, OHR, NIHTC
Marguerite Klein, ODS, NIH
Mengfei Huan, NIAID
Isis Mikhail, OCCAM, DCTD, NCI
Jenna Moran, OD, OHR, NIHTC
James Richards, OD, OHR, NIHTC
Kate Saylor, OD, OHR, NIHTC
Linda Southworth, CM, NCI

Debra Thangarajah, OD, OHR, NIHTC
Dan Xi, OCCAM, NCI

Members of the Public

Mary-Lynn Bender
Harry Gewanter
Richard Kotz
Douglas MacKay
Georgia Perdue
Taylor Walsh
Andrea Weiss
Robert Yates

I. Closed Session

The first portion of the 40th 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 229 applications were assigned to NCCAM. Of these, 73 were reviewed by NCCAM, 156 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 109 applications, requesting \$3,376,289 in total costs.

II. Open Session

The open session of the NACCAM meeting was called to order at 10:15 a.m. by Dr. Martin Goldrosen, NACCAM Executive Secretary.

Minutes from the Council meetings on June 2010 were unanimously approved, with no votes against and no abstentions. Dr. Goldrosen introduced Dr. Josephine Briggs, Director of NCCAM.

Report from the NCCAM Director

Acknowledgment of Retiring Members

Dr. Briggs thanked departing Council members Drs. Lori Alvord, Stephen Barnes, Boyd Bowden, Sheldon Cohen, and Margery Gass. She reported that a group of new candidates for membership has been submitted to HHS Secretary Dr Kathleen Sebelius.

National Institutes of Health (NIH) News

Dr. Briggs reported on five senior personnel changes at the National Institutes of Health and two of its Institutes. Dr. Lawrence Tabak has been named Principal Deputy Director of NIH, and Dr. Kathy Hudson has been named NIH Deputy Director. Dr. James Anderson is the new director of the NIH Division of Program Coordination, Planning, and Strategic Initiatives. Dr. Isabel

Garcia has been named new director of the National Institute for Dental and Craniofacial Research. Dr. Alan Guttmacher has been appointed director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. A search committee is performing ongoing work to fill the post of Director of the National Heart, Lung, and Blood Institute.

Dr. Briggs described her two new trans-NIH responsibilities: membership on the NIH Steering Committee, the most senior governing board at the NIH, and on that committee's Information Technology Working Group.

Staff Update

Dr. Briggs introduced six new NCCAM staff members Christina Brachna, public health analyst, OPPE; Cindy Caughman, scientific program analyst, OPPE; Nilesh Kalyanaraman, AAAS fellow, OPPE; Jennifer Kraszewski, program analyst, OCRA; Hungi Shau, scientific review administrator, DEA; and Barbara Stussman, survey Statistician, DER and reported one departure, Mr Ned Cullhane, scientific program analyst, DER who was accepted into the prestigious Presidential Management Fellows program.

Research Centers Update

Dr. Briggs announced five new Botanical Research Centers that will study the safety, effectiveness, and biological action of botanical products. These centers are being jointly funded by NCCAM, the NIH Office of Dietary Supplements, and, for two centers, the National Cancer Institute. The competitive awards were made to Pennington Biomedical Research Center, Baton Rouge, LA; University of Illinois at Chicago; University of Illinois at Urbana-Champaign; University of Missouri, Columbia; and Wake Forest University Health Sciences, Winston-Salem, NC.

Budget Update

Dr. Briggs presented budget information for Fiscal Year (FY) 2011. The President's budget request for NIH is \$32.0 billion, representing a 3.2 percent increase over the FY 2010 enacted level. The requested budget for NCCAM is \$132.0 million, representing a 2.5 percent increase over the FY 2010 enacted level. She also mentioned several recent congressional committee actions relevant to the FY 2011 budget.

Legislative Update

Dr. Briggs reported on a meeting she had with Senator Bernard Sanders (I-VT), and that at his invitation she will speak at a town hall meeting in Vermont on October 16, 2010.

She also discussed a U.S. District Court ruling on August 24, 2010, to halt federally funded research that uses human embryonic stem cells. The number of NIH grants affected is as follows: 143 grants (totaling \$95 million) that are now up for annual renewal will be frozen, as will 22 grants (totaling \$54 million) whose existing research is coming up for renewal in September 2010. One hundred thirty-one grants awarded this year are "out the door" and will not be affected unless they are due for renewal in a year.

Outreach Update

Dr. Briggs highlighted several examples of papers on NCCAM-funded research that have received national media attention, including a new paper on tai chi for fibromyalgia and an

accompanying editorial in the *New England Journal of Medicine* (08/19/10). They indicate, Dr. Briggs said, the high level of public interest in CAM and the importance of NIH's and NCCAM's existence and work.

On its Web site, NCCAM is beginning to develop more portal pages on specific topics--for example, on creatine, a dietary supplement used to enhance performance and build muscle mass in athletes. Creatine has troubling side effects, however, and there have been recent reports of contaminated creatine supplements. As illustrated in its creatine portal, the Center seeks to ensure balance and objectivity in all its outreach materials.

Dr. Briggs said that she continues to reach out to diverse stakeholders, through talks at the George Washington Institute for Spirituality and Health, World Pharma 2010, and the American Association of Naturopathic Physicians.

Upcoming Events

The lecturer for the next Stephen E. Straus Distinguished Lecture, on December 15, 2010, will be Dr. Vika Sukhatme of Harvard Medical School. Dr. Sukhatme will speak on "Promise for the Future in Yesterday's Remedies: Traditional Therapies to Modern Medicine."

NCCAM Strategic Planning Update

Dr. Briggs and Dr. Jack Killen, Deputy Director of NCCAM, led a discussion on the Center's strategic planning process. Publication of the strategic plan is planned for February 2011.

Dr. Briggs opened by presenting four major themes that have emerged in the strategic planning process. During discussion of each theme, Dr. Briggs referred to a "CAM Research Paradigm" model (basic science, translational research, efficacy studies, and effectiveness research).

The first theme was that the Center should have **greater research focus** in order to maximize its impact, and should select interventions with the greatest promise. Two of the promising areas that have emerged are symptoms (e.g., of pain, arthralgias, or stress-associated) and healthy behaviors. Dr. Briggs briefly took time at this point to discuss the peer review process, particularly the role of the Council in a more focused approach.

Discussion. There was support by Council for a more focused approach. Among the comments were suggestions to investigate chronic disease management over time, including how people learn to live well with their chronic condition(s) in a healthy way; including prevention, wellness, and health promotion; and leaving some funding room for other options, as for beginning investigators and for investigator-initiated ideas.

The second theme was **mechanisms and translational tools** --i.e., building a stronger understanding of mechanisms of action, and obtaining more and better translational tools to build the evidence base. This theme is important, Dr. Killen said, in order to be able to enter efficacy or effectiveness studies with a hypothesis that can be tested, to really know what one is doing, to be able to measure, and to obtain answer(s) that are as valid as possible.

With respect to mechanisms, Dr. Briggs showed a continuum model for markers: first, a "biological signature" (i.e., a marker of effect); second, a biomarker (validated as a correlate with patient benefit); and third, a "surrogate marker" (validated as being causally related to outcome). This need for information on mechanisms holds even though the relationship between efficacy and mechanism is often a "chicken-egg quandary," and even though many CAM modalities are complex and have numerous components.

With respect to translational tools, some examples of needed tools related to mind-body interventions were provided: treatment algorithms, measures of fidelity, measures of adherence, dose, validated subjective and objective outcome measures, and contextual factors.

Discussion. Among the comments expressed by Council members was that the biomarker challenge is formidable; it would be important to understand the process and to obtain biomarkers that are truly helpful. Dr. Briggs noted that many grant applications to date have proposed to move right into efficacy studies, and thus the theme under discussion would represent a shift in NCCAM's portfolio. There was a suggestion that this theme could be one for the field to sort out in making arguments for funding support, rather than NCCAM potentially having to define everything, potentially having a narrowing effect. The approach needs to be non-exclusionary, including elements such as the effects of treatment context and practitioner.

Following a break for lunch, Dr. Briggs reconvened the meeting at 1:30 p.m.

The third major theme to emerge from NCCAM's strategic planning process is that of strengthening **real-world effectiveness research** in NCCAM's portfolio--i.e., attempting to capture how CAM practices are used and how they work, in real-world settings. Dr. Briggs noted that effectiveness research--and the question of what strategies will be most effective in helping to inform health policy--is currently an active area of discussion across the NIH. This type of research would be useful in obtaining information to expand the evidence base, including on whole systems.

Discussion. Among points discussed were ways NCCAM could leverage resources and experience, contain costs, build research capacity (for example, among CAM providers and at CAM schools), and obtain many dimensions of information. It was emphasized that CAM therapies are being widely used, and part of NCCAM's mission is to help elucidate their value. One challenge is that these practices are quite variable. The theme speaks of an opportunity to try some things that are different, such as focusing on participants--for example, developing a more comprehensive approach to evaluating their individual aspects. Clinicians should be trained in research, including in how to frame a researchable question. There was a suggestion of large planning grants that would involve multiple investigators and multiple sites.

The fourth major theme was **communication**. The Council discussed whether the strategic plan draft has established a sound foundation for a coherent, compelling, and forward-looking communication strategy. Dr. Killen presented some proposed language--e.g., that "NCCAM pursues promising scientific opportunities to improve strategies for addressing compelling, unmet needs in health care and promotion, through state-of-the-art multidisciplinary research. NCCAM is rigorously objective and impartial in interpreting and presenting the evidence base about usefulness and safety." As two current examples, the Center is strengthening its information for health care providers and is looking into offering a tool on herb-drug interactions.

Discussion. Among the comments by Council members on this theme was that NCCAM needs to communicate that there are compelling reasons that rigorous research is done on CAM--for example, Americans spend \$34 billion per year on CAM, and NCCAM-funded research has an impact on American pattern of dietary supplement use. The overall goal is to present the research fairly and transparently. NCCAM's achievements should continue to be highlighted. Dr. Briggs noted that NCCAM's role is to help people be healthier.

Dr. Briggs thanked the Council for all its input on the draft strategic plan and said that the comments will be used to fine-tune the draft.

III. Mini-Symposium: NCCAM-Supported Research on the Biological Impact of Soy

The next segment was a mini-symposium on research on the biological impact of soy. Ms. Marguerite Klein of the NIH Office of Dietary Supplements opened the symposium with an introduction to soy and its components, the NIH interest in soy, and a few examples of scientific questions. Ms. Klein was the lead scientific planner of a 2009 NIH-sponsored workshop on designing, implementing, and reporting clinical studies of soy interventions.

Presentation by Dr. Stephen Barnes

Dr. Stephen Barnes of the University of Alabama-Birmingham spoke on "Challenges in Nutrition Research--Soy, Research, and Public Health Policy." Dr. Barnes's topics included the chemistry of soy and soy products; the variation in chemical composition in soy between studies and in commercial products; and soy in the Asian and Western diets. An important area to address in future clinical studies, Dr. Barnes said, is participants' previous exposure to soy, particularly in childhood and adolescence (as soy may have epigenetic effects). The microbiota of the gut contributes a great deal to human disease and human health, and is important in this research area as well, as in production of equol. One question to explore further is whether animal models are optimal for soy studies, since many convert daidzin/daidzein to equol at a much higher rate than do humans.

Presentation by Dr. Kenneth Setchell

Dr. Kenneth Setchell, of the University of Cincinnati College of Medicine, presented "Overview of Soy Isoflavone Metabolism, with a Focus on Equol."

Dr. Setchell's research includes proposal of an "equol hypothesis," that there may be advantages for people to "make" equol. Equol was first isolated from the urine of pregnant mares in 1932. In 1982, daidzin and daidzein, which are isoflavones in soy, were discovered to be the precursors of equol as studied in human urine. Equol is exclusively a product of intestinal bacterial metabolism; is not made in germ-free animals, or in human infants under 4 months old; and is not made by all humans who consume soy (e.g., about one-quarter of U.S. adults who eat one serving of soy per day make equol--a percentage that is higher in vegetarians--compared with about 50 to 60 percent of adults in China and Japan). Contrary to a popular belief, equol and soy isoflavones are not "estrogens" in the strictest sense--rather, they are closer to the class of SERMs (*selective estrogen receptor modulators*), such as tamoxifen and raloxifene, in the way that they bind to estrogen receptors and in their actions.

Equol and soy isoflavones have a wide range of biological activities, including some that make them intriguing targets for investigation for potential preventive and/or treatment effects in certain hormone-related conditions. For example, Dr. Setchell discussed his NCCAM-funded work on the chemopreventive effects of two equol enantiomers (R-equol and S-equol) in an animal model of breast cancer--including on timing of exposure to dietary equol.

Presentation by Dr. Howard Hodis

Dr. Howard Hodis, of the Keck School of Medicine of the University of Southern California, presented on an NCCAM-funded study that he has been leading, the Women's Isoflavone Soy Health Trial (WISH). Dr. Hodis's team is studying the intake of soy isoflavones on the development of vascular disease and multiple other health outcomes.

WISH is a carefully-designed long-term, double-blind, randomized controlled trial in healthy postmenopausal women without preexisting cardiovascular disease or diabetes mellitus. The endpoint is progression of subclinical atherosclerosis; specific outcomes include testing in seven cognitive domains, longitudinal change in bone mineral density, and mammographic density change. The trial is yielding a large data set that offers many opportunities for analysis.

Dr. Briggs praised the WISH study's successes to date and commented that it is a type of study that not only answers the primary question but yields a large data set that can be used to answer many other questions, foreseen and unforeseen.

IV. Public Comment Session and Closing

Dr. Harry Gewanter, representing the American Academy of Pediatrics' section on Complementary and Integrative Medicine, updated Council on recent activities of the section.

Dr. Briggs thanked the Council members and adjourned the meeting at 4:15 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
Complementary and Alternative
Medicine

Josephine Briggs, M.D.
Chairperson
National Advisory Council for
Complementary and Alternative
Medicine