

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CENTER FOR COMPLEMENTARY
AND INTEGRATIVE HEALTH**

**NATIONAL ADVISORY COUNCIL FOR COMPLEMENTARY
AND INTEGRATIVE HEALTH
MINUTES OF THE SEVENTY-THIRD MEETING
February 7, 2020**

NACCIH Members Present

Dr. Belinda Anderson, West Long Branch, NJ
Dr. Todd Braver, St. Louis, MO
Dr. Lynn DeBar, Seattle, WA
Dr. Robert Cichewicz,^{1,3} Norman, OK
Dr. Anthony Delitto, Pittsburgh, PA
Dr. Roni Evans, Minneapolis, MN
Dr. Diana Fishbein, University Park, PA
Dr. Joel Greenspan, Baltimore, MD
Dr. Richard Harris, Ann Arbor, MI
Dr. Kendi Hensel,¹ Fort Worth, TX
Dr. William (Bill) Helferich,^{1,3} Urbana, IL
Dr. Jean King, Worcester, MA
Dr. Benjamin Kligler,² Washington, DC
Dr. John MacMillan, Santa Cruz, CA
Dr. Wolf Mehling, San Francisco, CA
Dr. Eric Schoomaker,² Bethesda, MD
Dr. Lynne Shinto, Portland, OR
Dr. Justin Sonnenburg,¹ Stanford, CA
Dr. Barbara Timmermann,¹ Lawrence, KS
Dr. Gloria Yeh,¹ Boston, MD

¹Telephone

²Ex-officio

³Ad-hoc

NACCIH Members Not Present

Dr. Tammy Born Huizenga, Grand Rapids, MI

Non-NACCIH, Federal Staff Present

Dr. Barbara Sorkin, Office of Dietary Supplements, NIH

Dr. William (Bill) Elwood, Office of Behavioral and Social Sciences Research, NIH

Members of the Public

Ms. Roslyn Hennessy

Ms. Azadeh Ghadiri Mogheddam

Mr. Mohammed Mehdi Sangaefidi
Mr. Taylor Walsh

I. Closed Session

The first portion of the seventy-third meeting of the National Advisory Council for Complementary and Integrative Health (NACCIH) 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 172 applications were assigned to NACCIH. 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 92 scored applications, which requested \$42,842,216 in total costs.

II. Call To Order and Review of Council Operating Procedures

The open session convened at 10:15 a.m. Dr. Partap Khalsa, NACCIH Executive Secretary, called the meeting to order. The minutes of the September 2019 Council meeting were approved unanimously.

As required by the Council charter, the annual review of Council operating procedures was conducted. Dr. Khalsa presented the procedures for secondary review of grant applications, NACCIH reports to Council, Council review of concepts for research initiatives, appeals and appeal criteria, and Council involvement in policy and research priorities. Council approved the operating procedures unanimously.

III. NACCIH Director's Report

NACCIH Director Dr. Helene Langevin noted that the past year, her first as director, has been momentous for NACCIH, with the Center's 20th anniversary and the start of the strategic planning process. She thanked Dr. William Helferich and Dr. Robert Cichewicz, who participated in the closed session as ad hoc reviewers, and welcomed a new ex-officio Council member, Dr. Benjamin Kligler of the Department of Veterans Affairs (VA). New NACCIH staff include Dr. Peter Murray, a program director in the Division of Extramural Research (DER).

All 11 National Institutes of Health (NIH)-Department of Defense-VA Pain Management Collaboratory grants have successfully completed their planning (UG3) phase and are transitioning to the implementation (UH3) phase. Dr. Langevin called this a tremendous accomplishment and pointed out that this program is an important one for NACCIH.

NACCIH has been a full partner in the Helping to End Addiction Long-term InitiativeSM, or the NIH HEAL InitiativeSM. The governance structure of this initiative reflects its cross-institutional nature and allows for important collaborations. Almost \$1 billion dollars in funds were awarded this past year; this will be followed by \$500 million per year of sustained investment. HEAL recently held its first investigator meeting, where its broad scope was palpable. NACCIH is leading two major initiatives within HEAL: PRISM (Pragmatic and Implementation Studies for

the Management of Pain to Reduce Opioid Prescribing), which supports 5 pragmatic trials embedded in health care systems, and BRIM (Behavioral Research to Improve Medication-Based Treatment), which has funded 10 projects. One of the PRISM projects, a collaboration with the Centers for Medicare and Medicaid Services (CMS), is investigating acupuncture for chronic low-back pain in older adults. The CMS had planned to base its coverage determination on the results of this trial but recently made the decision to cover acupuncture for Medicare patients with chronic low-back pain. The trial remains extremely important.

NIH is continuing its efforts in three important areas: enhancing workforce diversity, addressing the issue of foreign influence, and increasing anti-harassment efforts.

NCCIH had a budget increase from Fiscal Years (FY) 2019 to 2020, which allows for expansion of the research program. NCCIH also enhances its impact by leveraging funds from other institutes, centers, and offices (ICOs) and other Federal partners. In FY 2019, NCCIH was budgeted \$102 million but accessed another \$43 million in special initiatives and \$19 million in cofunding from other ICOs. Investments from other Federal sources are particularly important for the HEAL Initiative projects, the NIH-DoD-VA Pain Management Collaboratory, the Health Care Systems Research Collaboratory, and the Sound Health Initiative research grants.

NCCIH is following developments regarding the possible expansion of acceptable sources of cannabis products for research. There seems to be bipartisan support for allowing researchers to study products that consumers actually use, rather than only allowing use of products made available through the National Institute on Drug Abuse, but there are no new developments at this time. NCCIH has funded 11 grants on minor cannabinoids and terpenes, and there will be future funding opportunities in this area.

Highlights of recently published NCCIH-funded research include:

- A paper from Dr. Yarimar Carrasquillo's group in the NCCIH Division of Intramural Research showing how the central amygdala functions as a pain rheostat.
- A paper from a multicenter team cofunded with the National Institute of Diabetes and Digestive and Kidney Diseases that demonstrated interactions between nociceptors and the gut immune system that could play a role in the defense against pathogens.
- A study, cofunded with the National Institute of Arthritis and Musculoskeletal and Skin Diseases, in which dietary supplements containing a mixture of polyphenols reduced disc degeneration pain in a rat model.
- An analysis of Medicare data that suggested that access to chiropractic care may reduce medical spending on services for spine conditions among older adults.
- A paper from NCCIH statisticians showing that more than 50 percent of physicians recommend complementary health approaches to patients during office visits, with female physicians recommending them at a higher rate than male physicians.
- A study from NCCIH's Office of Communications and Public Liaison that analyzed Twitter conversations on pain and compared them to conversations on cancer. For pain, patient conversations on nondrug pain management were completely separate from conversations among providers.

Dr. Langevin drew Council's attention to two current funding opportunities—the reissue of PRISM and a U24 for high-priority research networks on emotional well-being—both of which

will have preapplication webinars in the coming weeks. She also mentioned two notices of special interest (NOSIs) for existing funding opportunity announcements (FOAs)—one on mechanisms underlying pain-relieving properties of cannabinoids and terpenes and one on Alzheimer’s disease-focused administrative supplements for grants not presently focused on Alzheimer’s disease.

Recent NCCIH events include the 20th anniversary celebration, a videocast of which is available, and an NCCIH-hosted day-long satellite workshop on implementation and deimplementation methodologies for complementary and integrative health approaches, which was held in conjunction with the Science of Dissemination and Implementation in Health annual conference in December 2019. Upcoming events include ramping up of strategic planning activities, beginning with a webinar on whole person health concepts; the spring 2020 Integrative Medicine Research Lecture Series, on mental health, pain, and addiction; the 2020 International Congress on Integrative Medicine and Health (ICIMH), where NCCIH-led sessions include a town hall meeting on the Center’s strategic vision for 2021 and beyond; and a workshop on myofascial pain to be held in late summer/early fall 2020.

IV. Concept Clearance: Integrating Basic Behavioral and Social Sciences Training for Midcareer Investigators

Dr. Lanay Mudd, NCCIH program director and training officer, and Dr. Bill Ellwood, health scientist administrator and OppNet coordinator at the NIH Office of Behavioral and Social Sciences Research, presented a concept that would involve both NCCIH and OppNet (the NIH Basic Behavioral and Social Science Opportunity Network), a trans-NIH collaboration that accelerates discoveries in basic behavioral and social sciences research.

NCCIH has a long history of participating with OppNet on initiatives for midcareer enhancement through mentored cross-training and collaboration. Dr. Mudd and Dr. Ellwood presented several examples of previous award recipients who successfully expanded their research programs, gained new skills, established new research collaborations, and enhanced their careers through these opportunities.

The proposed initiative would provide training and career development opportunities to midcareer investigators who seek to expand their research programs by acquiring new skills and knowledge in the areas of basic psychological processes, sociological processes, or biomedical pathways, enabling them to go beyond and enhance their current areas of expertise. The initiative would support OppNet’s training interests and align with NCCIH’s interest in supporting transdisciplinary training at this career stage.

A motion to approve the concept was made, seconded, and passed unanimously.

V. Concept Clearance: Quantitative Evaluations of Myofascial Tissues: Potential Impact on Musculoskeletal Pain Research

Dr. Wen Chen, chief of the basic and mechanistic research branch in NCCIH’s DER, explained that musculoskeletal pain is one of the main driving forces for long-term use of opioids, and that between 30 and 85 percent of musculoskeletal pain patients have pain that may originate from the muscles or fascia. Substantial research investments have focused on the roles of the skeletal system and nervous system in musculoskeletal pain, but the roles of the muscles and connective

tissues are understudied. Currently, myofascial pain is diagnosed by history and physical examination (including palpation of tender foci), and no objective methods of diagnosis or validated nonpharmacologic treatments are available.

This HEAL Initiative proposal would support the development of improved quantitative evaluations, such as imaging, biopsies, and electromyographic recording, of muscles and fasciae to advance research on the pathophysiology and treatment of musculoskeletal pain. Examples of areas where research is needed include ultrasound sonoelastography and magnetic resonance elastography. The initiative, which would follow and build on the HEAL-approved FY 2020 workshop “Quantitative Evaluations of Myofascial Tissues: Potential Impact on Musculoskeletal Pain Research,” would include two phases. Phase 1 would focus on technology development and validation, and Phase 2 would focus on testing of nonpharmacologic treatments and other nonaddictive therapies. Potential treatments include acupuncture or dry needling, injections, manual therapies, and other complementary and integrative health approaches. It will be important to see whether the methods developed in Phase 1 can be used in Phase 2. This area of research has the potential to transform the treatment of a large group of patients and lead to less use of opioids.

Discussion: In response to a question from Dr. Harris about whether this initiative would be open to Eastern medicine techniques such as cupping, Dr. Chen explained that any intervention that would impact the muscles or fasciae would be relevant. In response to a question from Dr. Fishbein about whether the use of gabapentin and other drugs that decrease the excitability of nerves could be included, Dr. Chen explained that this initiative would primarily focus on nonneural tissues rather than nerves.

Dr. Schoomaker expressed concern that overly focusing on macro-level quantitative measurement might cause subtle signaling across fascial planes to be overlooked and that negative results might be incorrectly interpreted as invalidating the role of the fasciae. Dr. Kligler added that palpation should not be rejected as a guide to treatment. Dr. Langevin explained that the hope with this initiative is to be able to measure changes in tissue such as stiffness more subtle changes may also be going on and will be discussed at the workshop. Other techniques could look at more biochemical aspects of events in the fasciae, but this initiative would focus on noninvasive studies.

Dr. Anderson suggested that the conceptual framework of Chinese medicine could be valuable in interpreting results of palpation. Dr. King suggested that computational techniques could be valuable in Phase 1 as well as Phase 2, and Dr. Chen explained that they could be included in both phases.

A motion to approve the concept was made, seconded, and passed unanimously.

VI. Concept Clearance: Functional Neural Circuits in Interoception Science

Dr. Chen presented this concept, which represents a collective effort across many NIH agencies involved in the NIH Blueprint for Neuroscience Research consortium. Interoception is the process by which the body senses, interprets, integrates, and regulates signals from within itself.

The current portfolio of NIH-funded research on interoception emphasizes therapeutics rather than signaling and connections with the brain. This gap in the portfolio can be explained by the

scopes of the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative and the Common Fund's Stimulating Peripheral Activity To Relieve Conditions (SPARC) initiative, neither of which includes brain-body connections.

This initiative is intended to address that gap by focusing on the neural pathways (cranial, vagal, or spinal) connecting the brain with the rest of the body. The emphasis is on functional neural circuitry analysis of the complete neural circuits connecting the brain with the rest of the body via neural pathways in animal models. Key research topics could include but are not restricted to cell-type characterization of the peripheral ganglia involved in interoception, identification of specific ganglia responsive to interoceptive signals, anatomical mapping of neural circuits involved in interoception, and functional characterization of interoceptive circuits at the physiological and behavioral levels.

Discussion: In response to a question from Dr. Braver about why this initiative would be limited to animal models, Dr. Chen responded that a decision was made to focus on basic science first to have a better understanding of the circuits and support future clinical and translational efforts. Dr. Mehling commented that using animal models to study proprioception is difficult because some species, such as rats, have a very underdeveloped anterior insula. Dr. Schoemaker suggested that future efforts should look at unrecognized connections such as those between brain and bone marrow. Dr. Chen said that this initiative would not necessarily focus on already-recognized connections but could also try to discover new ones. Dr. Mehling asked whether pain is considered part of interoception, and Dr. Chen explained that pain cuts across both exteroception and interoception. Dr. Langevin commented that one thing missing in the musculoskeletal field is a better understanding of proprioception. In response to a question from Dr. DeBar, Dr. Chen noted that this initiative would be a trans-NIH effort.

A motion to approve the concept was made, seconded, and passed unanimously.

VII. Concept Clearance: Underlying Mechanisms of Force-Based Manipulations: High-Priority Research Networks

The term “force-based manipulations” refers to the application of mechanical force to the outside of the body with therapeutic intent. Examples include light touch, pressure, thrust, and needling. Fundamental understanding of the mechanisms of these manipulations is under-developed.

Much research has been done on force-based mechanosensation, but researchers in this field may not be aware of the relevance of their work to force-based manipulations. To bring these researchers together with those who study manual therapies, NCCIH and other NIH agencies held a roundtable discussion in September 2019. The roundtable participants identified research gaps and opportunities that included the need to characterize and quantify the types of forces; develop reliable measures of force, stress, strain, and stiffness; identify metrics and biomarkers for short- and long-term therapeutic responses; develop methodologies for applying and quantifying forces; develop technologies for real-time recording and imaging of cells and tissues during force-based manipulations; define and quantify psychosocial and expectation effects relevant to force-based manipulations; link therapy to multiscale response; and develop opportunities to connect neuroscientists, engineers, and clinician-scientists.

The proposed initiative aims to solicit applications that focus on developing resources in this field through meetings, conferences, small-scale pilot research, multidisciplinary cross-training (such as intensive workshops, summer institutes, or visiting scholar programs), and information dissemination in the following high-priority research areas: terminology and measurement, mechanistic research on the neural circuitry of force-based manipulations, contextual effects, biomarkers of force-based manipulations, and technology and methodology development for mechanistic studies.

Discussion: Dr. Mehling asked whether the focus and quality of attention from the practitioner are relevant to the contextual framework of force-based manipulations. Dr. Sabri said they are definitely important and noted that Dr. Catherine Bushnell, scientific director of NCCIH's DIR, has done research that shows that attention is an integral part of the circuitry. Dr. Schoomaker said that looking at the role of the provider is important. Dr. Hensel said it is important to distinguish spinal manipulation from osteopathic manipulation, which includes techniques other than thrust and does not just focus on the spine. Dr. Sabri said that force-based manipulations could include light touch and pressure and noted the need to develop common terminology for the manipulations used. Dr. Hensel explained that chiropractic manipulation and osteopathic manipulation are not the same, and all manual therapies should not be lumped together. Dr. Langevin said that NCCIH is interested in differences as well as similarities among force-based manipulations. Dr. Hensel said that osteopathic manipulation should be represented in the initiative. Dr. Evans expressed approval of including psychosocial factors in the model, stating that there is more to treatments than just manipulation. Dr. Delitto commented positively on the cross-disciplinary nature of the initiative.

A motion to approve the concept was made, seconded, and passed unanimously.

VIII. Symposium on Clinical Trials Oversight

NCCIH Deputy Director Dr. David Shurtleff opened the symposium on clinical trials oversight, noting that NIH has launched initiatives to enhance the transparency of clinical research and that NCCIH has been involved in this area for a long time. The goal is to facilitate a rigorous, robust clinical research portfolio. Dr. Langevin added that she hoped for a dialogue between NCCIH and Council members so that each could better appreciate the other's point of view.

NIH Policy and Overview

Dr. Michael Lauer, NIH Deputy Director for Extramural Research, explained that efforts to review how NIH oversees clinical trials were catalyzed by a 2012 Yale University publication. This paper indicated that the main results of only about 50 percent of NIH-funded clinical trials registered in clinicaltrials.gov were published within 2½ years. The Yale authors noted that no policies existed to ensure public access to results of unpublished NIH-funded research. NIH initially assumed that this analysis was methodologically flawed because it was expected that investigators would be highly motivated to publish their research. The National Heart, Lung, and Blood Institute (NHLBI) then conducted its own investigation of cardiovascular trials to try to clarify the situation. The NHLBI analysis essentially replicated the findings of the Yale study and provided some additional insights, including a higher rate of prompt publication for trials with hard clinical endpoints than those with surrogate endpoints. A 2016 paper from the Yale group found that institutions varied in the percentage of trials that had results reported within 2

years of completion, but most ranged between 30 and 40 percent for total clinical trials (not just those funded by NIH).

Another issue, identified by the U.S. Government Accountability Office, is that NIH was limited in its ability to function as a steward of clinical trials because not all relevant data were collected and no process had been established for using data on clinical trial activity to enhance stewardship.

In response, NIH has put multiple new policies in place including a new definition of clinical trials, a requirement for NIH staff who oversee clinical trials to complete good clinical practice training, creation of clinical trial-specific FOAs to ensure appropriate review, and a requirement that all NIH-funded clinical trials must be registered and reported. Results must be reported within 1 year after study completion, either in a journal or on clinicaltrials.gov. Scientists have an ethical obligation to disseminate results of trials involving human subjects out of respect for the burden and risk experienced by the study participants. Other changes to enhance clinical trials stewardship and enable systems change include the establishment of a single Institutional Review Board (IRB) policy for multicenter trials, grant application form changes, and creation of a protocol template for trials involving products regulated by the U.S. Food and Drug Administration (FDA).

Dr. Lauer explained that basic experimental studies with human participants have been a focus of NIH attention because clinicaltrials.gov is not always a suitable platform for studies of this type. NIH has relaxed the requirement for registration and reporting of these trials by allowing investigators to use alternative platforms. Another area where some flexibility is allowed is the single IRB policy; some exceptions have been granted. Enhancing the stewardship of clinical trials is an ongoing process, and more remains to be done.

Discussion: In response to a question from Dr. Fishbein, Dr. Lauer explained that in general, trials with negative findings are less likely to be published, but in the NHLBI cohort of studies, this pattern was not observed. However, analysis of the NHLBI-funded studies was difficult because complete information was not available on the results of unpublished trials. One pattern observed in the NHLBI data was that studies with better methodological quality were published more rapidly irrespective of results. Methodological quality reflects factors that can be assessed at the time of the initial proposal, such as the methods used for randomization and blinding. This is an additional impetus for using FOAs that are specific to clinical trials.

NCCIH Implementation of Clinical Trials Oversight – Background and Data

Dr. Shurtleff noted that NCCIH has been very serious about oversight of clinical research, and that oversight is a partnership between DER and the Office of Clinical and Regulatory Affairs (OCRA).

Dr. Emmeline Edwards, director of DER, discussed that NCCIH's portfolio includes more clinical research than the NIH average. Sixty percent of NCCIH's extramural research is clinical; the NIH average is 40 percent. The NCCIH clinical research portfolio is robust and diverse. It includes diverse study designs and grant mechanisms that have expanded over time. Trials fall into three partially overlapping groups: mind and body, natural products, and outcomes and effectiveness. The principles for oversight of the clinical portfolio are to minimize risk to

participants; maximize the success, scientific potential, and impact of funded work; and maximize productivity and mission-relevance of NCCIH programs. These principles are particularly important to NCCIH because the Center studies health interventions that are widely used by the American public, often with insufficient evidence on efficacy and safety.

Clinical trials in the early NCCIH portfolio had two common limitations: (1) Most were single-site studies, with limited generalizability. It was not clear whether the intervention could be delivered with fidelity in other settings. (2) Many trials failed to demonstrate the hypothesized benefit, and useful information could not be gleaned from the trials because key building blocks were lacking. For example, it was often unclear whether participants had received enough of the treatment and whether the duration and frequency of the intervention were appropriate. For natural product studies, it was often unclear whether the right product had been selected.

NCCIH currently uses a framework for research that spans the continuum from basic and mechanistic research through translational studies, intervention refinement and optimization, efficacy/effectiveness trials, and pragmatic studies and dissemination. This sequence provides specific FOAs for all stages of research, allowing investigators to have opportunities to develop the necessary building blocks before conducting large-scale trials.

Dr. Catherine Meyers, director of OCRA, described the success of the clinical trial enterprise as reliant upon public trust in scientific rigor, transparency, and ethical oversight. NIH, the largest Federal funder of clinical trials, shares the responsibility of stewardship with investigators and their institutions. NCCIH takes the responsibility of stewardship very seriously and has a spectrum of oversight activities. Some trials receive routine oversight and others receive enhanced oversight. Routine oversight includes pre-award NCCIH staff discussion, and discussions and written communication with the principal investigator (PI), and collection of post-award accrual information. Enhanced oversight includes all the elements of routine oversight plus study document submission to NCCIH and in some instances, on-site monitoring. In 2011-2014, a very high percentage of NCCIH clinical trials, about 80 to 90 percent, received enhanced oversight. More recently, the proportion of trials receiving enhanced oversight has decreased to 20 to 30 percent, with enhanced oversight targeted primarily at larger and more complex studies.

Discussion: In response to a question from Dr. Schoemaker, Dr. Edwards and Dr. Meyers explained that there is a process for taking into account past experience with a particular PI or institution, including experience with previous clinical trials funded by NCCIH. Dr. DeBar said that some pragmatic trial parameters do not fit easily into clinicaltrials.gov; single IRB processing is challenging; and it does not eliminate the need for individual sites to adhere to state regulations. Dr. Meyers said that the single IRB process has not necessarily reduced the administrative burden and complexity of oversight but has made the inclusion of large numbers of centers in a trial more feasible.

Dr. DeBar commented that standardization of FOAs from different NIH agencies could be helpful. Dr. Lauer said that efforts are being made to reduce repetitive questions in FOAs and related forms. He explained that it should be possible, starting in 2022-2023, to begin to analyze the impact of clinical trial policy changes that went into effect in 2018. In response to a question from Dr. Evans, Dr. Lauer explained that delays in publication of studies may reflect investigators' desire to have their studies published in the most appropriate journals or delays in

journal review and publication. One reason why the option of reporting results in clinicaltrials.gov is offered is that studies cannot be rejected. There have been discussions with journal editors about whether reporting results in clinicaltrials.gov constitutes prior publication, but no satisfactory answer has been reached.

Dr. Shurtleff said that the traditional R01 funding mechanism may not be optimal for clinical trials. The two-stage UG3/UH3 process may be better because it builds in start-up time. Dr. Edwards and Dr. Meyers noted that the R21 funding mechanism may not provide enough money or time for a clinical trial. Dr. King cited an instance where resources ended before a project ended and pointed out that with recent increases in oversight, investigators are asked to complete additional tasks, which exacerbates this type of problem. Dr. Shurtleff said that tremendous strides are being made in thinking about how best to fund clinical trials, and tailored funding mechanisms are now available. Dr. Mehling said that the R61 mechanism has problems with inadequate money and time. Dr. Shurtleff explained that the R61/R33 mechanism is designed to give investigators a chance to try something novel and innovative, and it is expected to have a high risk of not transitioning to the second stage, unlike the UG3/UH3 mechanism, which has a high transition rate. Dr. King said that mechanisms for additional funding under appropriate circumstances, not just no-cost extensions, would be helpful.

Dr. Langevin acknowledged the complexity of clinical trials funding and policies and asked for feedback on whether NCCIH is communicating effectively with investigators on these topics. Dr. Shurtleff added that a partnership exists between NIH and investigators. The perspectives of both are important.

NCCIH Implementation of Clinical Trials Oversight – Award Processes

Dr. Edwards reviewed the pre-award process, which involves staff work and collaboration between DER and OCRA, including discussions of study aims, analytic plans, recruitment plans, and data safety and monitoring plans (DSMPs). The primary emphasis is on maximizing study rigor and impact as well as feasibility. At the pre-award stage, NCCIH sends the PI a clarification letter, which includes a request for information about milestones (for transition grants), requests for the DSMP and study accrual and retention plan (SARP), and a reminder of other requirements if an award is made. If enhanced oversight is planned, additional information is requested for that purpose. Post-award, the oversight process includes SARP and monitoring report submissions for all studies and additional submissions for enhanced oversight studies.

Dr. Meyers noted that the on-site monitoring program began in earnest in 2012 and is consistent with the overall oversight strategy. Monitors verify safety, data integrity, and compliance with requirements. NCCIH is reviewing this program to ensure it is applied to the most appropriate projects.

NCCIH's SARP allows clarification of the timeline of a project before implementation and enables early recognition of accrual problems and early outreach. NCCIH has a long history of collecting interim accrual reports; SARP now allows this information to be collected in an electronic format. The purpose of SARP is not to limit the ability of studies to be completed; instead, the goal is to intervene early enough to make a difference so that studies can be finished.

Web-based NCCIH resources for clinical trials include the Clinical Research Toolbox, which is updated frequently. The Toolbox includes information on the on-site monitoring program, resources for startup, and milestone documents for transitional grants, among many other resources.

Discussion: In response to questions from Dr. Anderson, Dr. Meyers said that data to evaluate the impact of reducing enhanced oversight are being collected, but results are not available yet. Concerns that oversight would delay studies have proven unfounded; rather, the attention and timelines involved in oversight tend to keep projects moving. Dr. Evans said SARP is a wonderful tool, but there have been a few issues with the electronic reporting. She also suggested that on-site monitoring might be made voluntary in some instances. Dr. Meyers said that NIH-wide information technology changes, such as a recent SharePoint upgrade, led to issues with SARP and NCCIH is carefully tracking these issues.

Dr. Shurtleff and Dr. Evans both suggested that on-site monitoring could be performed virtually in some cases. Dr. Meyers said that followup visits are often done virtually, and there have been discussions with the on-site monitoring contractor about doing initial visits virtually in some instances.

Dr. Harris said that from his viewpoint as a former basic researcher who transitioned into clinical research, it would have been helpful to have more training on the clinical trials process. Junior investigators may not realize that getting the award is only one hurdle. Dr. Shurtleff suggested that institutions could take on this training, and NIH staff could come in and talk about clinical trials oversight. Dr. Harris noted that training on oversight could also be helpful for Council members. Dr. Shurtleff said that institutional training at the predoctoral and postdoctoral levels should include these topics. NIH can provide resources, but the institution must be open to expanding the curriculum. NIH's role in oversight could also be added to existing training on pragmatic research.

Dr. Edwards said that one-shot workshops on clinical trials oversight have been held at ICIMH, but a more sustained effort may be needed. Dr. Mudd said that clinical trials oversight will be included in NCCIH's workshop on career development and transitions at ICIMH this year. Dr. Meyers pointed out that other agencies involved in clinical trials, such as FDA and the Centers for Disease Control and Prevention, could also get involved in training.

Dr. Harris said that it is difficult to fit some types of outcomes into the clinicaltrials.gov format, which is designed for efficacy trials. Dr. Braver noted that even senior investigators may need training before conducting their first clinical trial. Dr. Wendy Weber, chief of the clinical research branch in DER, noted that much information about the steps investigators need to follow is provided in a checklist in the Just-in-Time letter. Dr. Evans said that despite print resources, investigators sometimes get lost in the oversight process, and having a "buddy" to guide them could be helpful.

Dr. Langevin asked whether Council members thought the amount of back-and-forth involved in oversight might be too much. Dr. Delitto said that problems occur when new steps are added that do not fit into a project's budget. Dr. Evans said that the oversight process improves research, but the lack of latitude in project budgets is a problem. Dr. Timmermann suggested that PIs who have clinical trials funded by NCCIH might benefit from having a mechanism to get together

with one another. Dr. Meyers said that a model like that exists for larger cooperative agreement groups but not for smaller projects.

Dr. Shurtleff saw a common theme that investigators need to know in advance what they are getting into when they propose a clinical trial. Dr. Anderson pointed out that the hurdles would be even greater for complementary and integrative health institutions than for research-oriented institutions. Dr. Yeh said that based on her experience conducting a study with on-site monitoring, she found the full discussion and explanation included in the oversight process helpful. Giving investigators this information early on—including the rationale—would help everyone be on the same page. Dr. Hensel agreed that having better resources available to clarify the clinical trial oversight process—such as webinars and workshops—would be helpful, especially for novice investigators. Dr. Shurtleff said NCCIH would follow up on Council members’ suggestions. Dr. Langevin thanked Council for the informative discussion.

IX. Public Comment and Adjournment

Ms. Azadeh Ghadiri Mogheddam from COSMOintel, Inc. explained that Faradarmani is a type of complementary therapy with a mystic perspective and part of a larger theory developed by Mr. Mohammad Ali Taheri. It is based on the theory of a conscious bond that leads to healing of the body and psyche. In this therapy, the patient is connected to the cosmic consciousness network—the intelligence and awareness governing the universe. Faradarmani comes from an ultra-holistic viewpoint. According to this perspective, man’s existence is seen as being as vast as the universe and includes various energy transformers (chakras) and other, unidentified parts.

Mr. Mohammed Mehdi Sangaefidi discussed research with a cosmic consciousness base related to the theories of founder Mr. Mohammad Ali Taheri. Mr. Sangaefidi described it as the first time in human history that humans can use the cosmic consciousness network through a repeatable, testable scientific theory. He stated that subcategories of this mysticism are used as drug-free complementary medicine by about 1 million people in Iran.

The meeting was adjourned at 3:30 p.m.

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

Partap Khalsa, D.C., Ph.D., D.A.B.C.O.
Executive Secretary
National Advisory Council for
Complementary and Integrative
Health

Helene Langevin, M.D.
Chairperson
National Advisory Council for
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