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 Eighty-Fourth Meeting
May 12, 2023

NACCIH Members Present
Dr. Helene Benveniste, New Haven, CT
Dr. Per Gunnar Brolinson, Blacksburg, VA
Dr. Nadja Cech, Greensboro, NC
Dr. Robert Coghill, Cincinnati, OH
Dr. Daniel Dickerson, Los Angeles, CA
Dr. Helen Lavretsky, Los Angeles, CA
Dr. James Russell Linderman, Captain, Navy, Bethesda, MD*
Prof. Rhonda Magee, San Francisco, CA
Dr. Wolf Mehling, San Francisco, CA
Dr. Lynne Shinto, Portland, OR
Dr. Erica Sibinga, Baltimore, MD
Dr. Amala Soumyanath, Portland, OR

NACCIH Members Present Virtually
Dr. Todd Braver, St. Louis, MO
Dr. Anthony Delitto, Pittsburgh, PA
Dr. Margaret Haney, New York, NY
Dr. Girardin Jean-Louis, Miami, FL
Dr. Benjamin Kligler, Washington, DC*

NACCIH Members Not Present
Dr. Karen Sherman, Seattle, WA

*Ex Officio Member

I. Closed Session

The first portion of the eighty-fourth 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 1009 of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2). A total of 164 applications were assigned to the National Center for Complementary and Integrative Health (NCCIH). Applications that were noncompetitive, not discussed, or not recommended for further consideration by the scientific review groups were not considered by Council. Council agreed

with staff recommendations on 78 scored applications, which requested $37,705,767 in total costs.

II. Call to Order and Brief Review of Council Operating Procedures

Dr. Martina Schmidt, director of the NCCIH Division of Extramural Activities (DEA), convened the open session of this hybrid meeting at noon ET. The minutes of the January 2023 meeting were approved unanimously.

III. NCCIH Director's Welcome and NCCIH Report

Dr. Helene M. Langevin, director of NCCIH, welcomed all Council members. She acknowledged the recent death of Dr. Chao Hsing Yeh, UT Health Houston, who had served in many NCCIH review meetings, and praised her service to NCCIH.

Dr. Langevin presented a recent NIH-issued Request for Information (RFI): Re-envisioning U.S. Postdoctoral Research Training and Career Progression within the Biomedical Research Enterprise (NOT-OD-23-084). This was an opportunity to provide input on issues important to postdoctoral researchers, including working conditions, salaries, training, and future opportunities. NIH is currently analyzing the responses. She also talked about ARPA-H, which is hiring program managers. ARPA-H is geared toward rapid acceleration of developing technologies and translation to commercial development. Two focus areas (proactive health: keeping people from being patients; and resilient systems: building integrated healthcare systems) are in the same spirit as NCCIH's whole person health framework.

Dr. Langevin expressed her appreciation for the contributions of Ms. Lori Knutson, who recently stepped down from her role on Council. She welcomed six new Council members: Dr. Helene Benveniste, Yale School of Medicine; Dr. Per Gunnar Brolinson, Edward Via College of Osteopathic Medicine; Dr. Daniel Dickerson, University of California Los Angeles; Dr. Erica Sibinga, The Johns Hopkins University School of Medicine; Prof. Rhonda Magee, University of San Francisco; and CAPT James Russell Linderman, U.S. Department of Defense (ex-officio). Dr. Langevin congratulated Dr. Jessica McKlveen, who was promoted to director, NCCIH Office of Scientific Review. NCCIH is currently seeking a Facility Head to lead the activities of the NIH Pain Research Center. This position will help grow the field of pain research at NIH.

Dr. Langevin highlighted several FY 2023 budget updates, including $5 million earmarked for pain-related research; an increase from $19 million to $23 million in competing research projects; and a $1.5 million contribution to the National Health Interview Survey (NHIS). NCCIH has leveraged funds from other NIH Institutes/Centers (ICs) and trans-NIH initiatives. This includes a $26 million contribution from the NIH Helping to End Addiction Long-term® Initiative, or NIH HEAL Initiative®, of which $14 million is directed to myofascial pain and $3.4 million to behavioral and social interventions to improve medication-assisted treatment adherence for opioid use disorders.

Dr. Langevin announced a new NCCIH webpage, The NIH Music-Based Intervention Toolkit. This toolkit provides music and health researchers with resources, including core sets of common

data elements, functional outcome measures, and guidelines for future research. She also highlighted several publications on studies funded or co-funded by NCCIH:

- Radin RM, Epel ES, Mason AE, et al. Impact of digital meditation on work stress and health outcomes among adults with overweight: a randomized controlled trial. *PLoS One*. 2023;18(3):e0280808.
- Zahrt OH, Evans K, Murnane E, et al. Effects of wearable fitness trackers and activity adequacy mindsets of affect, behavior, and health: longitudinal randomized controlled trial. *Journal of Medical Internet Research*. 2023;25:e40529.
- Zamarripa CA, Spindle TR, Surujunarain R, et al. Assessment of orally administered Δ9-tetrahydrocannabinol when coadministered with cannabidiol on Δ9-tetrahydrocannabinol pharmacokinetics and pharmacodynamics in healthy adults: a randomized clinical trial. *JAMA Network Open*. 2023;6(2):e2254752.

Recent NCCIH-led or involved events include:

- 4th Annual NIH HEAL Initiative Investigator Meeting. February 21–22, 2023. Four significant initiatives related to musculoskeletal pain were presented. These initiatives are very important as NCCIH grows its portfolio on musculoskeletal pain research.
- Emotional Well-Being 2nd Annual Investigator Meeting. March 27, 2023. The keynote presentation by Dr. Tyler VanderWeele, Flourishing and Emotional Well-being, is available on the NIH Videocast website.
- U.S. Department of Veterans Affairs State of the Art Conference. March 29–30, 2023. "Measuring What Matters Most: Whole Person Outcomes." Dr. Langevin was keynote speaker.
- Hot Topic Webinars. Expanding Translationally Relevant Chemical Space: Insights Into Natural Product Resources, Technologies, and Mechanisms (Parts 1 and 2). March 6 and April 28, 2023 (available on the NCCIH website).
- Bridge to Artificial Intelligence (Bridge2AI) Consortium Meeting. April 17–19, 2023. Development of large-scale data sets ready for artificial intelligence (AI) that address difficult problems, such as salutogenesis.
- Arts and Wellness Panel with NeuroArts Blueprint. April 19, 2023. Discussion with Kennedy Center Artistic Advisor-at-Large, Renée Fleming. Dr. Emmeline Edwards, director of the Division of Extramural Research (DER), and Dr. Francis Collins, former NIH director, presented the NIH Music-Based Intervention Toolkit.
- NIH HEAL Initiative: 1st Annual PURPOSE (Positively Uniting Researchers of Pain to Opine, Synthesize, and Engage) Meeting for Early-Career Pain Researchers. May 11–13, 2023. Encouraging networking and mentoring among early-stage investigators.

Upcoming events include:

- Integrative Medicine Research Lecture: Unleashing the Power of Prevention to Enhance Well-Being Across the Lifespan. May 25, 2023. Margaret Kuklinski, Ph.D.

- Hot Topic Webinar. Launching a Career in Health Disparities Research—An NCCIH Perspective. June 7, 2023. Speakers: Dr. Eugene Dunne; Dr. Crystal Chapman Lambert; Dr. Shufang Sun.
- 9th Annual BRAIN Initiative Meeting. June 12–13, 2023.
- Integrative Medicine Research Lecture: New Insights Into Prevention and Management of Chronic Pain in Children and Adolescents. June 15, 2023. Tonya M. Palermo, Ph.D.
- 2023 IMAG Multiscale Modeling Consortium (MSM) Meeting. June 28–29, 2023.
- 2nd Annual Force-Based Manipulation Investigator Meeting. June 29, 2023. Keynote address: Dr. David Ginty. Updates from ForceNet, Neurons MTTR, and Spine-Work.
- Understanding and Restoring Whole Joint Health in Pain Management: An NIH HEAL Initiative Workshop. July 25–26, 2023. Virtual workshop.

Discussion: Dr. Edwards reported that the requests for applications have been issued for the Common Fund NIH Director's High-Risk, High-Reward Research Program. Prof. Magee asked about strategies for making research findings more accessible to the lay population, particularly, how to think about the effects and patterns of economic inequality. Additionally, she asked about the ethics of AI for health and well-being to move forward in a positive manner. Dr. Langevin explained that NCCIH takes communication very seriously and that packaging findings into an integrated body of knowledge is a big piece of whole person health. There has been tremendous positive response from the community on the concept of whole person health, including at the stakeholder meeting last fall with more than 100 organizations in attendance. Dr. Langevin said that AI is a very important topic throughout NIH and noted she is one of five IC directors on the Bridge2AI executive committee. One of the group's primary concerns is how to build an AI-ready data set that is ethically sound and ensures no built-in inequities in acquisition of data.

Dr. Jean-Louis supported introducing quantum computing to accelerate discoveries but recognized that such equipment can be very expensive. He asked if NIH is willing to support projects that are asking for funding to build such programs. Dr. Langevin noted that requests for equipment must be made on a case-by-case basis. However, through the Office of Data Strategy (ODS), NIH is heavily invested in making sure investigators have tools and resources to move into the era of big data, including long-term data storage. NCCIH is engaged in conversations throughout NIH led by ODS and the National Library of Medicine to make sure we are moving forward as quickly and effectively as possible. Dr. Kligler thanked Dr. Langevin for mentioning the "Measuring What Matters Most" conference and said the VA is grateful for the partnership with NCCIH and the work being done to measure outcomes for whole person health.

Recognition of Retiring Council Members

Dr. Langevin recognized retiring Council members Drs. Diana Fishbein, Richard E. Harris, Tammy Born Huizenga, Roni Evans, Kendi Hensel, and Justin Sonnenburg.

IV. NIH HEAL Initiative: Update on NCCIH's Clinical Research Programs and Projects

A. Overview of HEAL Initiative Structure and Pain Research Clinical Programs

Dr. Wendy Weber, branch chief, Clinical Research Branch, DER, introduced the four focus areas of the NIH HEAL Initiative. Many of the topics addressed through the initiative relate to the NCCIH mission and vision, and NCCIH is pleased to be part of this initiative.

The primary goals of the initiative are to enhance pain management to reduce risks and needs of starting opioids, improve prevention and treatment strategies for opioid addiction and overdose, and examine chronic pain and opioid use. The number of people reporting chronic pain in the United States increased from 18.4 percent in 2011 to 20.4 percent in 2019, while those experiencing high-impact chronic pain rose from 4.8 percent in 2011 to 7.4 percent in 2019.

Since 2018, $2.5 billion has been awarded to more than 1,000 research projects. There are currently 314 clinical trials on addiction, overdose, and pain, of which more than 100 focus on back pain and 200 address medications for opioid use disorder (OUD). There are 41 U.S. Food and Drug Administration submissions for clinical testing of new drugs or devices.

Dr. Weber highlighted NIH HEAL Initiative programs that NCCIH oversees or is directly involved with, including Pragmatic and Implementation Studies for the Management of Pain to Reduce Opioid Prescribing (PRISM), the ERN (Effectiveness Research Network) program, Trial Innovation Network (TIN) Resources, the Advancing Health Equity Project, and the Secondary Data Analysis Project.

B. Overview of HEAL-Funded OUD Research Programs, Including BRIM

Dr. Peter Murray, program director, DER, introduced the Behavioral Research to Improve Medication-Based Treatment (BRIM) program, which looks at targeting medications for opioid use disorder (MOUD) adherence to improve long-term outcomes. Half of people in treatment programs drop out within the first 6 months. Timing of treatment varies, and MOUD may be needed for years to prevent relapse. Three dimensions are necessary for treatment adherence: initiation (starting the treatment regimen), implementation (executing the prescribed dosing schedule), and persistence (staying in treatment long enough to be successful).

Fourteen trials were accepted for the two-phase milestone-driven awards; all have transitioned to the second phase of funding. All studies are administered by NCCIH, with two transferring to the National Institute on Drug Abuse (NIDA) for the second phase. To date, six trials have published pilot study results, two have completed recruitment, and four have been awarded administrative supplements to add work that analyzes the role of stigma as an additional challenge to receiving MOUD. All studies focus on individuals with OUD, and four also include chronic pain.

Dr. Murray presented an update on Integrative Management of chronic Pain and OUD for Whole Recovery (IMPOWR), which is administered by NIDA with secondary support from NCCIH. The "whole recovery" element goes beyond treatment of the condition and includes the context for how or why it exists, such as stigma, health disparities, and comorbid psychiatric conditions.

Both MOUD and complementary and integrative therapies are effective treatments separately for OUD and chronic pain, but much less is known about combining them to treat both. Treatment is fragmented, and patients typically receive care for OUD and chronic pain from different

providers. Resources, expertise, and communication between providers are often limited. The increase of opioid-related overdoses during COVID-19 added another challenge to research.

IMPOWR's vision is to generate evidence-based, patient-centered solutions for integrated management of co-occurring chronic pain and OUD and rapidly disseminate knowledge to impact population health. To do this, these interventions need to be implemented across diverse settings, focus on the whole patient, acknowledge inequities, engage research partners and people with lived experience, and give special consideration to early-stage investigators.

HEAL is implementing a national K12 mentoring career program to identify and train a diverse pool of clinical pain researchers. Guidelines will be developed to maximize mentoring and career development, with the goal of helping the scholars transition to successful careers. The program will collaborate with PURPOSE. A funding opportunity was previously announced, and the first three scholars will participate in a "training bootcamp" during the summer.

C. OPTIMUM Trials Engagement of Stakeholders Using a Community Advisory Board

Dr. Natalia Morone, associate professor of medicine, Boston University, presented her work with the Optimizing Pain Treatment in Medical Settings Using Mindfulness (OPTIMUM) study. OPTIMUM is a pragmatic randomized clinical trial, with a 1-year follow-up, that integrates telehealth group-based mindfulness-based stress reduction programs into primary care settings for people with low-back pain. The study is recruiting 450 participants over the age of 18. The three health care systems participating are Boston Medical Center, UPMC at the University of Pittsburgh, and the University of North Carolina at Chapel Hill, including Piedmont Health Services, a Federally Qualified Health Center. To date, 366 people have been randomized.

The intervention group (n = 225) will participate in 8 weekly 90-minute group-based mindfulness sessions, while the control group (n = 225) will receive usual primary care. Interested patients will be screened for eligibility and complete a baseline survey. Participants will complete additional surveys after 8 weeks, 6 months, and 12 months.

The community advisory board (CAB) has 10 members, including patients, mindfulness instructors, health care professionals, pain advocacy group leaders, and administrators. They provide feedback and advice on issues such as low-back pain, ways to engage providers and participants, how to provide mindfulness, how to tailor study recruitment, and next steps for after the study. CAB members were trained on the research process as well as their roles as partners in the study using Connecting Community to Research: A Toolkit, developed by Boston Medical Center. Dr. Morone shared examples of changes in recruitment materials based on CAB feedback. Pictures of people in pain or holding their backs were replaced with images from nature, and clear descriptions of mindfulness, eligibility for the study, confidentiality language, and benefits of participating in the study replaced vague language.

Discussion: Dr. Benveniste asked if the investigators can test that the participants are actually (and accurately) doing mindfulness activities. Dr. Morone said the primary provider checks in with participants and asks for specific descriptions of the mindfulness activities they are using. Dr. Coghill thanked Dr. Morone for sharing the patient feedback about shaping and improving

materials. He noted that he is in the process of updating materials and will ask for patient feedback. Dr. Morone said she found the feedback surprising but incredibly valuable.

D. Mindfulness Oriented Recovery Enhancement (MORE) as an Adjunct to Methadone Treatment for Opioid Use and Chronic Pain

Dr. Nina Cooperman, associate professor of psychiatry, Rutgers University, discussed the findings from two MORE studies. While methadone treatment (MT) is the most common MOUD in the United States, about 50 percent of people who begin MT discontinue within 1 year. Of those who remain in treatment, 50 percent relapse within 6 months. This may be due to chronic emotional and physical pain that needs to be addressed. A study published in *JAMA Internal Medicine* last year found that MORE reduced opioid misuse at 9 months by 45 percent.

MORE is an 8-session group intervention that includes mindfulness, cognitive reappraisal, and positive emotion regulation skills. It targets dysfunctional cognitive, affective, and behavioral pathways that lead to relapse. MORE has been found to be useful for alcohol addiction, illicit drug use, smoking, obesity, and internet addiction. The two studies Dr. Cooperman presented were the first to evaluate MORE among people with an OUD, in treatment, and on any MOUD. Both studies were based in methadone clinics in New Jersey, and participants were recruited by clinic staff. To be eligible, participants had to be currently on MT, experiencing chronic pain, and able to attend the sessions. Participants were randomized in blocks of 14. Surveys were conducted at baseline, at 8 weeks, and 16 weeks.

The small pilot study (n = 30) evaluated the feasibility of implementing MORE in MT settings. Participants with chronic pain were randomized to MORE (n = 15) or methadone treatment as usual (MTAU) (n = 15). The MORE group reported significantly fewer days of drug use than the MTAU group. The MORE group also had significantly better pain-related functioning, less anxiety, and less depression. In the second study, 154 participants were randomized to MORE (n = 77) or MTAU (n = 77). Due to COVID-19, the study was implemented virtually, and participants received smartphones to respond to prompts. The study found 36 percent fewer days of drug use with MORE than with MTAU, particularly opioid use. MORE participants had a significantly longer time to relapse over 16 weeks. Additionally, people in the MORE group had greater adherence to MT (4.4 times) at 16 weeks, greater reduction in pain intensity and depression, and slight reduction in anxiety compared to MTAU. Both studies concluded that MORE is an efficacious intervention for addressing substance use, pain, and mental health and improving MT outcomes.

Dr. Cooperman also described two new studies of MORE—a Type 2 hybrid implementation and effectiveness study in methadone clinics and a study of MORE for non-illicit polysubstance use, including alcohol and tobacco use, as well as a pending study that will translate MORE to prevent opioid misuse in primary care populations.

Discussion: Dr. Benveniste asked if the use of buprenorphine as an alternative to methadone and the potential of methadone clinics closing in some areas around the country are concerns for the future of these studies. Dr. Cooperman said that in her area, methadone clinics are not going away, but her research team is working to translate their intervention into various treatment

models. Mindfulness interventions are being investigated in outpatient settings where buprenorphine is provided. Additionally, work being done in primary care settings with MORE can be helpful with increasing awareness of and adherence to other MOUDs.

Dr. Dickerson asked about the mindfulness structure and which exercises are implemented. Dr. Cooperman explained there are 2-hour group sessions over 8 weeks of intervention, which incorporate mindful breathing and mindful savoring of positive experiences. Dr. Sibinga asked if they will study outcomes for a longer period. Dr. Cooperman confirmed there will be 6- and 12-month follow-up. She is also exploring how to help participants maintain mindfulness practices. Dr. Sibinga asked for more details about clinician training. Dr. Cooperman explained that focus groups and advisory boards will be incorporated to get input from clinicians and patients to better understand how to integrate this into the treatment setting. They are also comparing the full mindfulness package that requires training to a simple script, which can be read to guide participants through mindfulness exercises to gauge effectiveness. Dr. Jean-Louis asked if they are finding a relationship between mindfulness and sleep quality, and if it is a buffer to better improvement in outcomes. Dr. Cooperman confirmed sleep assessments are included.

Professor Magee asked if the control group includes group interaction so that the effect can be isolated to measure if mindfulness or being part of the group relates to improvement. She also asked if interpersonal mindfulness practices and compassion affect outcome. Dr. Cooperman explained that her research team abstracted all additional group and individual psychotherapy time and treatment from the patients' charts at the clinics and did not find any significant differences in psychosocial intervention between the MTAU and MORE groups. Additionally, many of the MTAU participants were already participating in groups at the clinics, and MORE replaced those group interactions. As for interpersonal connections, in the MORE group there is a processing component and a support component as part of the group experience that allows for doing the experiential exercises together.

Dr. Shurtleff asked if adherence rates in the MORE group translated to other aspects of participants' life, such as job performance or family relationships. He also asked if there were any changes in cravings. Dr. Cooperman explained that because the study occurred during COVID-19 and many people were unemployed, they don't have specific measures on those outcomes. They do have well-being and coping skills outcomes but haven't analyzed them yet. They did look at cravings in the pilot study. Individuals in the MORE group reported experiencing more cravings and were more aware of the cravings, but they were more likely to cope with them. All the data from the R33 study have not been analyzed yet.

Dr. Haney asked if the takeaway is that people in substance use treatment are open to mindfulness, which Dr. Cooperman confirmed. Dr. Weber commented that a speaker at a NIH HEAL Initiative investigators meeting shared that there is a high incidence of staff burnout and staff turnover at their OUD clinic. Implementing mindfulness programs for staff transformed their clinic. Dr. Cooperman noted that training for the intervention is experiential, and it is recommended that clinicians practice the intervention as well to hopefully change the culture toward mindfulness.

Dr. Weber summarized the presentations, noting that the patterns of drug use are shifting and there are new threats, such as xylazine, known as "tranq," which is more deadly than fentanyl. The NIH HEAL Initiative is looking at polysubstance use in relation to addiction and overdose. Other issues include getting real-time data to better identify a new crisis; addressing co-occurring issues; and examining the relationship of sleep, OUD, and mental health. Unfortunately, pain management is still fragmented and health inequities for both pain and addiction persist. The role of social determinants in getting treatment is an area the NIH HEAL Initiative is considering. She shared the initiative's resources for funding opportunities and funded projects.

V. Concept Clearances

1. Whole Person Research Initiative

Dr. Emrin Horgusluoglu, program director in DER's Basic and Mechanistic Research Branch, and Dr. Elizabeth Ginexi, program director in DER's Clinical Research Branch, presented the Whole Person Research Initiative concept. NCCIH's current strategic plan defines whole person research as including three components: 1) exploring the fundamental science of interconnected systems; 2) investigating multicomponent interventions or therapeutic systems; and 3) examining the impact of these interventions on multisystem or multiorgan outcomes.

In September 2021, NCCIH, along with other ICs, convened a workshop that explored potentially appropriate methodologies for whole person research. Dr. Horgusluoglu noted that several themes emerged, including that a focus on a single disease, condition, or body part will not be sufficient to solve major health problems in the United States, and a single-modality intervention is often not enough to manage complex medical and health conditions.

Dr. Ginexi explained that the Whole Person Research Initiative will aim to create dedicated multidisciplinary research programs that will develop and test state-of-the-art research models through innovative study designs, computational methods, and analytical models to quantitatively study, represent, simulate, and analyze the effects of multicomponent interventions on the interconnected physiological systems of the whole person with diverse social and environmental contexts. Examples of activities may include building interconnected networks of multidisciplinary researchers, creating an overarching coordinating center to facilitate collaboration across the initiative, and supporting efficacy and effectiveness trials that could be based on research models developed earlier in the initiative.

Discussion: Dr. Cech asked if the studies would involve basic and mechanistic science and clinical work, or if those would be separate. Dr. Ginexi replied that this is a collaborative effort with a broad-ranging scope and will require input from both groups of researchers. The first step is bringing all the relevant expertise together. Dr. Lavretsky asked if the studies will address systems that are responsive to a single intervention or if they will have multicomponent interventions targeting different systems. Dr. Horgusluoglu said that because more information is needed to develop the methodology, they could start with the question, "What is the impact of single interventions on multiple organ systems?" Dr. Lavretsky said that a similar concept was used by the National Institute on Mental Health (NIMH) in the Research Domain Criteria

Initiative (RDoC) assessment. Dr. Ginexi agreed that RDoC is a good example. Dr. Horgusluoglu added they hope to identify the root condition in single organ systems and not just multiple organs. Dr. Brolinson voiced support of this concept, commenting that practitioners use multicomponent practices with patients, whether treating an acute or chronic illness. This approach is especially used in sports medicine. Dr. Dickerson commented that in Native American studies he looks for different types of assessments—mental, physical, spiritual—to capture different domains.

Prof. Magee asked if there is a whole community or collective conceptualization of what whole health requires. Dr. Ginexi acknowledged that NIH researchers sometimes fall short on the community side. As an applied social scientist, she will provide that lens to this project and hopes to build models that can bring that to bear. One of the biggest predictors of health in this country is ZIP Code and ignoring that would be remiss. Dr. Langevin said NCCIH has many NIH partners who are very interested in collaborating, including the National Institute of Nursing Research, National Institute of Environmental Health Sciences, and National Institute on Minority Health and Health Disparities. Council voted on the concept and approved it as presented.

2. Resource Center for Cannabis and Cannabinoid Research

Dr. Patrick Still, program director in DER's Basic and Mechanistic Research Branch, introduced a concept for a cannabis research resource center, noting that 37 states have legalized medical and/or recreational use of cannabis despite uncertainty about short- and long-term health effects. In October 2022, NCCIH hosted a principal investigators' meeting where awardees discussed challenges in cannabis research including the need for increased funding; increased clinical grade products, tools, standards, and metrics; and guidance on regulatory requirements. These challenges intersect with those of several other NIH ICs involved in cannabis research, who have expressed interest in partnerships.

The proposed center will include three core areas: 1) Regulatory Compliance Core to provide regulatory information and act as a clearinghouse; 2) Analytics Core to store best practices and resources; and 3) Outreach and Community Support Core for conducting public and scientific outreach, administering seed funding, and assisting with the navigation of U.S. Food and Drug Administration (FDA)/ Drug Enforcement Administration (DEA) regulatory requirements for application development. These core areas and objectives will be interconnected, assisting investigators at every career stage.

Discussion: Dr. Cech asked if low and high tetrahydrocannabinol (THC) products will be included. Dr. Still explained that this center will distinguish between the two and will provide guidance for both as well as regulatory guidance on the need for Schedule 1 clearance. The current FDA guidance points researchers to different routes, depending on THC concentration levels, and the center could help researchers determine how to proceed. Dr. Cech also asked if the center will be led by NIH or if investigators will submit applications to create the center. Dr. Still replied that it will be a cooperative agreement with NIH oversight. The center will be led by an investigative team, and outreach and meeting support will be led by the community.

Dr. Benveniste commented that without more background information it seemed difficult to appreciate the extent of the program. She acknowledged that she is new to Council and the process but suggested that more advance information about concepts could be helpful. Dr. Shurtleff said that providing extensive detail at this stage would be getting ahead of the process. He explained the goal is to decide if the concept is worth supporting and if it will benefit public health. Dr. Schmidt and Dr. Langevin acknowledged that the concept presentations may sound broad at this stage. Dr. Schmidt reminded the group that there is information about the concepts in the Electronic Council Book. Dr. Langevin said that the comments are appreciated and that providing a synopsis in advance will be considered for future meetings.

Returning to the discussion of the concept, Dr. Shurtleff reiterated that cannabis research is far behind public use, and regulatory restrictions for researchers are daunting. Dr. Haney said that funding for cannabis studies is difficult to secure. She also mentioned that some disease-focused institutes are not conducting research on cannabis despite its known use by some patients. She asked for clarification on the center's role for accessing the products to be studied. Dr. Still said that the center would provide resources to the research community about how to access the needed product for study. Dr. Shurtleff agreed that more data on how cannabis is being used by the public is needed, and as more states legalize cannabis, the more NIH is taking notice to establish more research opportunities. He said NCCIH believes the coordinating center will facilitate the work. Dr. Mehling congratulated NCCIH on exploring this for all ICs. Council voted on the concept and approved it as presented.

3. Enhancing Mechanistic Research on Precision Probiotic Therapies

Dr. Hye-Sook Kim, program director in the DER's Basic and Mechanistic Research Branch, introduced the concept by highlighting the potential benefits of probiotics, including improvement of mental health and metabolic disorders and modulating the immune system. While *in vitro* and *in vivo* studies have demonstrated beneficial effects and mechanisms of action, these preclinical results have not translated to clinical trials, which presents a challenge to probiotic research. One solution is to develop a procedure that would predict interindividual variations and tailor probiotic strains to individual-specific features. However, this approach requires an understanding of the variabilities of probiotic responses on an individual level and an innovative tool to address these complexities.

In April 2022, NCCIH and the Office of Dietary Supplements held a workshop with 10 NIH ICs and the U.S. Department of Agriculture to identify research priorities, gaps, and opportunities. Clinical trials have not captured the complex patterns of the gut microbiome, host genetic variability, dietary differences, or environmental exposures of both microbes and hosts between individuals. There has been a lack of effective translation to robust mechanistic studies to test causality. Additionally, advanced computation and AI approaches are needed to interrogate intricate relationships between multiple complex systems. Based on these findings, the concept proposes highly innovative mechanistic research to develop probiotic interventions with a two-phase approach. Phase 1 will be an observational clinical study or secondary data analysis to rigorously assess the microbiome and map the person-specific factors, and then develop a computational analysis and AI tools for determining critical factors to identify patient

subpopulations. Phase 2 will use the gathered data and design animal and human mechanistic studies to test for causality. Examples of research topics include identifying novel biomarkers for diagnosis and prognosis, looking into mechanisms of action and the factors that interfere with treatment, identifying new targets for intended probiotic effects, and developing new probiotic strains.

Discussion: CAPT Linderman asked if Phase 1 will take a longitudinal approach when looking at the individual differences or if it will be a single sample from the population. Dr. Kim said that they are more interested in longitudinal sampling so they can determine patterns instead of cross-sectional features to identify links to probiotic efficacy. Dr. Soumyanath asked what aspects of human biology they intend to examine. Dr. Kim said they will look at everything, including diet, immune system, host genomes, and use of medication, as these are all factors that influence the probiotic response. Dr. Lavretsky said that other microbiome researchers cannot define a gold standard due to various influences, including diet. She asked how these studies will leverage the data to establish what is "normal" or "healthy." Dr. Kim explained they are not looking to define "normal" or "healthy," and Phase 1 will look at factors other than immune response, such as individuals' microbiome and how that will influence the probiotic. Dr. Mehling asked if they will look at the influence of different diets, and Dr. Kim confirmed that will be studied. They hope to develop the computation with the AI tool to tease apart and find the best probiotic strains for different diets. Council voted on the concept and approved it as presented.

VI. Public Comments

Written comments can be submitted to Dr. Schmidt by email (Martina.Schmidt@nih.gov) or postal mail (address on the NCCIH website) within 15 days after the meeting. Comments may be up to 750 words. A public comment was received ahead of the meeting, proposing a spiritual component be incorporated into NCCIH's framework for whole person health as a separate domain. Council discussed this suggestion during the closed session.

VIX. Final Remarks and Adjournment

Dr. Schmidt thanked Council and NCCIH staff. NCCIH would not be able to pursue its mission without Council's expertise and feedback. Dr. Langevin added her thanks to NCCIH staff and thanked Council for their input and feedback. The meeting adjourned at 3:29 p.m.

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

Martina Schmidt, Ph.D. Executive Secretary National Advisory Council for Complementary and Integrative Health	Helene M. Langevin, M.D. Chairperson National Advisory Council for Complementary and Integrative Health