PREPARED STATEMENT OF HELENE LANGEVIN, M.D. DIRECTOR, NATIONAL CENTER FOR COMPLEMENTARY AND INTEGRATIVE HEALTH

The mission of National Center for Complementary and Integrative Health (NCCIH) is to define, through rigorous scientific investigation, the safety and effectiveness of complementary and integrative health approaches, which are a group of practices and products that originate outside of conventional medicine. This diverse group of health practices includes natural products such as dietary supplements, plant-based products, and probiotics, as well as mind-body approaches such as yoga, massage therapy, meditation, mindfulness-based stress reduction, spinal manipulation, and acupuncture. According to a 2012 National Health Interview Survey (NHIS), Americans are spending approximately \$30.2 billion a year on complementary approaches to improve their overall health, manage symptoms of chronic diseases, and/or counter the side effects of conventional medicine. However, the scientific research base surrounding the safety and efficacy of these practices is limited. Therefore, NCCIH is committed to providing the American public with valuable information about these practices, while also investigating how specific complementary approaches can be integrated into conventional medical care.

EXPLORING NONPHARMACOLOGIC APPROACHES FOR PAIN MANAGEMENT

NCCIH is devoting significant resources to understand the basis of pain and how complementary and integrative health approaches can be utilized in pain management. Pain is a major public health problem and is the most common reason Americans turn to complementary and integrative health practices. Data from the 2012 NHIS found that an estimated 25.3 million adults in the U.S. (11.2 percent) experience daily pain with nearly 40 million adults (17.6 percent) experiencing severe levels of pain. The use of highly addictive opioids as a primary pain management strategy in the U.S. is helping to fuel the growing opioid misuse epidemic. Improved strategies for pain management may lead to a decreased reliance on opioids for patients suffering from pain. NCCIH supports research to better understand the biologic mechanisms of pain and to identify effective nonpharmacologic approaches to reduce the duration and intensity of pain.

Research supported at NCCIH is focused on understanding the role of the brain in perceiving, modifying, and managing pain, with the long-term goal of improving clinical management of chronic pain through the integration of pharmacologic and nonpharmacologic approaches. Recently, scientists discovered a new class of sensory nerve cells that respond to high-threshold (intense) mechanical stimuli, such as hair pulling. This work provides insights into how our bodies encode and transmit pain sensations. Another study mapped the regions of the brain activated during pain to establish a "pain signature" and found that specific regions of the brain respond to pain intensity, while other regions mediate the psychological effect, and yet another region showed increased activity related to pain relief. This work not only provides insights

into how pain is interpreted, but could lead to the development of new methods to detect, quantify, or target pain.

NCCIH-supported research is also advancing understanding of the mechanisms of action of mind and body interventions and determining their effectiveness for treating pain. One study investigated the effect of acupuncture on carpal tunnel syndrome and found that it affected activity within brain pain centers, decreased associated pain symptoms, and improved overall wrist function. Mindfulness meditation is another promising area of research. Numerous studies have shown that mindfulness meditation helps relieve pain, but the mechanism through which meditation exerts this effect is not well known. New study results demonstrate that mindfulness meditation activates the same region of the brain as opioids; however, it reduces pain independently of opioid neurotransmitter mechanisms. These results suggest that greater pain control could be achieved through the combination of mindfulness meditation and opioid-signalinginduced pharmacologic approaches. NCCIH-supported research has also shown that mindfulness-based stress reduction and cognitive behavioral therapy can improve functioning and reduce chronic low back pain in young and middle-aged adults and may provide patients with skills for long-term management of pain. Studies have demonstrated that these approaches resulted in substantial cost savings over usual care.

ADVANCING RESEARCH ON NATURAL PRODUCTS

According to the 2012 NHIS, nearly one in five U.S. adults use botanical supplements and other non-vitamin, non-mineral dietary supplements, such as fish oil/omega-3 fatty acids and probiotics. Adverse events related to dietary supplements are estimated to contribute to 23,000 emergency department visits in the U.S. each year. To better inform consumers and their health care providers, NCCIH supports rigorous research on the biological mechanisms of the benefits and potential harmful effects of natural products with the goal of improving the body of knowledge available to health care providers and patients.

NCCIH is supporting a Center of Excellence to determine how best to study potential adverse interactions between natural products and conventional medications. The goal is to develop a definitive approach to determine the clinical relevance of supplement-drug interactions to inform design of future research and, ultimately, decision-making about using natural products and medications together.

In FY2015, NCCIH partnered with NIH's Office of Dietary Supplements (ODS) to establish the Centers for Advancing Research on Botanical and Other Natural Products (CARBON) Program. Through this program, researchers recently identified two chemicals found in grapes that could significantly reduce depression-like behaviors in mice. The systems targeted by these compounds are not the same as current pharmaceutical antidepressants and may provide novel insights into the biology of depression and could lead to new therapeutic agents. The program is also developing new methods for chemical characterization of natural product mixtures, biological profiling assays, and creating new informatic tools to rigorously analyze and share data.

NCCIH is also supporting research on cytisine, a natural product for smoking cessation. Despite promising results from clinical trials conducted outside the U.S., cytisine has not yet been approved for use in the U.S. NCCIH supported a series of preclinical studies on cytisine through a strategic collaboration with Achieve Life Sciences, Inc., OncoGenex Pharmaceutical, Inc., other NIH ICs, and private research organizations. Recently, the FDA accepted an Investigational New Drug application that permits phase 2 clinical studies to further assess cytisine as a smoking cessation treatment. This continuing public-private partnership may lead to the wide availability of a new option to address the major public health issues associated with tobacco use.

CONCLUSION

As a responsible steward of resources, NCCIH supports scientifically meritorious basic, mechanistic, clinical, and translational research. The Center focuses on areas with the greatest potential impact by prioritizing research topics that show scientific promise and are amenable to rigorous scientific inquiry. We leverage strategic partnerships to build the scientific evidence needed on the safety and efficacy of complementary health approaches and disseminate evidence-based information to the American public.

Helene Langevin, M.D.

Director, National Center for Complementary and Integrative Health

Helene Langevin, M.D., was sworn in as director of the National Center for Complementary and Integrative Health (NCCIH) on November 26, 2018. Prior to her arrival, she worked at the Osher Center for Integrative Medicine, jointly based at Brigham and Women's Hospital and Harvard Medical School, Boston. Dr. Langevin served as director of the Osher Center and professor-in-residence of medicine at Harvard Medical School since 2012. She has also served as a visiting professor of neurological sciences at the University of Vermont Larner College of Medicine, Burlington.

As the principal investigator of several NIH-funded studies, Dr. Langevin's research interests have centered around the role of connective tissue in chronic musculoskeletal pain and the mechanisms of acupuncture, manual, and movement-based therapies. Her more recent work has focused on the effects of stretching on inflammation resolution mechanisms within connective tissue. She has authored more than 70 original scientific papers and is a fellow of the American College of Physicians.

Dr. Langevin received an M.D. degree from McGill University, Montreal. She completed a postdoctoral research fellowship in neurochemistry at the MRC Neurochemical Pharmacology Unit in Cambridge, England, and a residency in internal medicine and fellowship in endocrinology and metabolism at The Johns Hopkins Hospital in Baltimore.

As NCCIH director, Dr. Langevin oversees the Federal government's lead agency for scientific research on the diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine. With an annual budget of approximately \$142 million, NCCIH funds and conducts research to help answer important scientific and public health questions about natural products, mind and body practices, and pain management. The center also coordinates and collaborates with other research institutes and Federal programs on research into complementary and integrative health.