

SCIENCE AND GOVERNMENT

In Defense of NCCAM

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The National Center for Complementary and Alternative Medicine (NCCAM) is one of the 27 institutes and centers that constitute the National Institutes of Health (NIH). Its mission is to investigate complementary and alternative medicine (CAM) in the context of rigorous science, to train CAM researchers, and to disseminate authoritative information to the public and professional communities. From its beginning, NCCAM has encountered controversy and strong sentiments for and against the scientific study of CAM, such as that appearing in this issue of *Science* (1) and elsewhere (2). Some criticisms have been valid and have led to more stringent policies on product quality and safety, for example. Others are misinformed. Our goal is to bring fact and clarity to this discussion, just as we seek to bring science to the assessment of CAM.

History of Establishing NCCAM

The U.S. Congress established NCCAM in 1998 to bring scientific rigor to studies of CAM by the same legislative process used to establish other NIH institutes and centers. This is a challenging mandate, one that required establishing a new CAM research enterprise that met the high standards of biomedical research for which NIH is known. NCCAM has outlined its approach to studying CAM in its 5-year strategic plans, the most recent of which was published in 2005 (3). These plans were developed with balanced debate and advice from a wide range of individuals representing the scientific community, conventional and CAM practitioners, and the public.

The criticism that only a handful of individuals have shaped the NCCAM agenda is not accurate. In creating our second strategic plan (3), NCCAM embarked on a year-long process of agenda-setting dialog. The center held a think tank of leading scholars, including three current and past NIH institute directors; convened stakeholder forums on the East and West coasts; assembled a strategic planning workshop with more than 80 individuals from mainstream medicine and CAM communities; and sought input from over 1500 individuals and professional organizations. We specifically included distinguished conventional scientists (without experience in CAM) to lend their expertise to discussions of CAM-related research challenges.

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Counterpoint: The National Center for Complementary and Alternative Medicine has successfully met the challenge of conducting difficult and controversial research.



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NCCAM Advisory Council and Peer Review

As with other institutes at NIH, the composition of the NCCAM Advisory Council was specified in congressional language. The council includes individuals with conventional scientific and medical training, such as M.D.'s and Ph.D.'s, and others with CAM expertise, as well as representatives from the lay public [see (4) for the current roster]. NCCAM's Advisory Council has scientists with exemplary records of accomplishment in a variety of disciplines. This balanced composition reflects NIH's interdisciplinary approach to today's complex scientific questions. The 17 current council members have published 414 peer-reviewed articles and received 35 NIH grants in the period from 2001 to 2006 (23 of which were awarded by other NIH institutes).

NCCAM's peer-review process is the same as other NIH institutes, i.e., content experts review applications in their area of expertise. Cardiologists review applications on ischemic

heart disease, and pharmacologists, including pharmacognosists, review applications on botanical products. NCCAM's investigator-initiated R01 grant applications are reviewed by study sections convened by the NIH Center for Scientific Review; thus, they compete on an even playing field with all other applications to NIH. All members of NIH peer-review panels and advisory councils, including those at NCCAM, adhere to NIH policies concerning conflict of interest. The NCCAM Advisory Council acts as a second level of review.

Product Quality and Patient Safety

One of the most challenging issues in studying CAM has been the quality of dietary supplement products available for research and the variability of quality and content of products in the marketplace. Unlike pharmaceutical firms, dietary supplement manufacturers do not have to establish efficacy before marketing their products to the public. The Food and Drug Administration (FDA) regulates dietary supplements as foods, not drugs. Therefore, FDA does not analyze the content of dietary supplements. Moreover, U.S. law does not define the term “standardized.” Thus, product quality and consistency can vary. This is a challenge for both researchers and the public.

NCCAM has developed a multifaceted strategy to ensure the quality of biologically active agents used in NCCAM-supported research.

Now, before NCCAM funds a project, a Product Quality Working Group, composed of pharmacologists, pharmacognosists, and other scientists, reviews information to determine whether the product is of the quality required to replicate research findings. Information is collected on more than 20 factors, including product characterization, standardization, contamination, consistency, and stability, that could affect the quality of research data. NCCAM also carries out quality-control assessments of random samples of biologically active products that are being used in the studies it funds. The selected samples are sent to independent laboratories for analysis, thus providing information on stability, quality, and characterization.

In addition to these product-quality measures, NCCAM has also established an independent phase I resource center to conduct preclinical pharmacology research on dietary supplements. In selecting candidate supplements for study, NCCAM places a priority on products that are widely used by the public, yet have insufficient data on factors such as dose range, bioequivalence, pharmacokinetics, bioavailability, and botanical-drug interaction—information that is currently lacking for many botanical products.

The safety of individuals participating in NCCAM-supported clinical studies is of paramount importance to the center. In addition to NIH-required safeguards for human subject protection, NCCAM has an Office of Clinical and Regulatory Affairs to provide oversight of NCCAM studies involving human subjects. This office oversees the Data and Safety Monitoring Boards for NCCAM's clinical trials and ensures compliance with Institutional Review Boards' guidance and FDA regulations. Other NIH institutes have similar offices. This research infrastructure has been created to ensure that the research that NCCAM funds will be reproducible and meet the rigorous standards expected by NIH-funded research.

NCCAM Research

In the early years of NCCAM, there was a sense of urgency to scientifically assess a range of CAM therapies that had been in long use by the public in the absence of proof of safety or efficacy. Thus, NCCAM undertook a number of clinical trials in its first years, many with support from other NIH institutes. In doing so, we have gained valuable experience that has informed our thinking about challenging issues in CAM research such as dosing, methodology, and other experimental factors.

When early trials of botanical products, such as saw palmetto, did not show efficacy, NCCAM focused attention on the doses used in these studies, which were based on those widely used by the public. NCCAM now has a policy of requiring dose-range studies and

other preclinical research before conducting clinical trials. The NCCAM research portfolio now includes more basic research focused on mechanisms of action, pharmacokinetics of herbal products, drug-herb interactions, and dose optimization, as well as clinical effects. This shift is reflected in the decline of the NCCAM clinical research portfolio from 80% in 2000 to 68% in 2005. The balance of basic and clinical research continues to serve the specific public health issues that NCCAM was created to address.

Contrary to the criticism that NCCAM prescribes areas of study to investigators, the center, like other NIH institutes, accepts unsolicited, investigator-initiated applications that are based on ideas formulated by the applicant, not NCCAM. The percentage of solicited grants funded by year varies, but in the last three fiscal years, about 87% of NCCAM-funded grants are unsolicited. NCCAM welcomes well-designed research applications on a wide range of CAM therapies.

Research Findings

In 2002, the National Health Interview Survey of more than 31,000 people found that 62% of Americans use some form of CAM (5). The public is using CAM without proof of efficacy or safety, which is the very reason that NCCAM-funded research is so important.

NCCAM's research has provided valuable information on the physiologic pathway of the placebo effect using state-of-the-art brain imaging technologies (6), the efficacy of acupuncture to relieve pain associated with osteoarthritis of the knee (7), and a potential role for glucosamine-chondroitin for patients with moderate-to-severe osteoarthritis pain (8). NCCAM's research is in the forefront of understanding the interactions of prescription drugs and dietary supplements (9). NCCAM's scrutiny of product safety informed the FDA's decision to withdraw ephedra from the marketplace (10).

These are a few examples of the more than 1000 peer-reviewed publications that have resulted from the first 7 years of basic and clinical research supported by NCCAM. NCCAM's research results will help build a fuller understanding of what CAM can offer. We not only expand our knowledge about the tested therapy but also learn more about the condition it is meant to treat. Overall, we should regard each study's results in the same way—as yet another crucial piece of the research puzzle.

Conclusion

After only 7 years, NCCAM has made important contributions in a field that is fraught with controversy and challenges. NCCAM is applying the same scientific standards to the conduct of research and its review as used by other NIH institutes. We have raised the bar on the

study design and methods used in CAM research, including the quality of products under investigation. Our portfolio of basic research will inform subsequent clinical studies to ensure that we are testing a high-quality product, at the optimal dose, and in the appropriate population.

Before the establishment of NCCAM, there was no central source of CAM information. NCCAM brings evidence-based information on CAM to the public, practitioners, and researchers. NCCAM disseminates research findings and provides reliable information about commonly used CAM practices through numerous channels, including its information clearinghouse and its award-winning Web site (11). NCCAM's communications program deals with a field that is controversial, that has many critics, and that reaches a public that wants reliable information.

We fully support the Institute of Medicine's (12) recommendation that the same principles and standards of evidence apply to all treatments, whether labeled as conventional medicine or CAM. We believe that we have succeeded in establishing a research enterprise that will achieve this standard. While challenges remain, we are confident that knowledge gained from NCCAM-supported studies will continue to inform the public, health-care providers, and policy-makers about how and when evidence-based CAM therapies should be used and effectively integrated into conventional medical care.

References

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