



**Council for Responsible Nutrition**<sup>®</sup>

*The Science Behind the Supplements*<sup>®</sup>

**Paper 1: NCCAM Mandate and Mission**

- 1. Major features of the current CAM research landscape that are important in considering future strategic directions for NCCAM and the field of CAM research in general.**

CRN Comment:

Early CAM research involving botanical and other natural products has suffered from poor characterization of test material. CRN supports the current NCCAM emphasis on proper characterization of test material used in clinical trials, which assists with reproducibility of results. We applaud initial efforts that NCCAM and the Office of Dietary Supplements (ODS) have taken to address this problem, and endorse the continued allocation of resources to this area.

- 2. Particular needs and opportunities of importance to NCCAM's efforts in research capacity building**

CRN Comment:

Clinical trials carried out using the development of chronic diseases as clinical endpoints are complex and costly. Therefore, CRN supports the allocation of NCCAM resources to assist in the development and validation of biomarkers as modifiable surrogate endpoints for both disease and “wellness”.

CAM interventions, such as consumption of adequate omega-3 fats, vitamin D, and lutein/zeaxanthin, have the potential to reduce the incidence of chronic diseases such as cardiovascular disease, cancer, and macular degeneration.

Implementation of clinical trials using surrogate endpoints, such as omega-3 cell membrane levels, inflammatory cytokines profiles, and macular pigment density could increase CAM research capacity globally, by providing the foundation for shorter and more cost effective intervention studies.

The examples given above are used to demonstrate the concept of validated biomarkers as surrogate endpoints and do not reflect any particular CRN priorities.

### **3. Opportunities, obstacles, and NCCAM's future role in supporting research on approaches to improved states of general health and well-being**

CRN Comment:

It is clearly a difficult task to define general health and well-being. A state of “well being” may in fact be different for each individual. CRN recommends exploring the definition of “wellness”, but cautions NCCAM against allocation of excess resources trying to answer such a complex question. Achieving consensus among scientists, integrated practitioners, and researchers on a definition of wellness is analogous to a group of psychologists and councilors to agree on a definition for happiness.

NCCAM resources may be better allocated identifying and validating multiple objective measures that are known contributors to general health and wellness, while recognizing that these measures are only small, but measurable pieces to a larger puzzle. General health could be defined as a combination of physical measurements (BMI, percent body fat, basal body temperature, blood pressure, etc.) and biomarkers (inflammatory profile, omega-3 index, serum 25-hydroxyvitamin D levels, macular pigment density, bone density, etc.). NCCAM may also benefit by exploring emerging measurements of health status such as metabonomics, or the quantitative measurement of the dynamic multiparametric metabolic response of living systems. Other state of the art “omic” (genomic, proteomic, and metabolomic) measurements may also contribute to better understanding complex integrative modalities. NCCAM is well positioned to display leadership in these areas through collaboration with other NIH centers.

Clinical trials that investigate multi component CAM treatment approaches, as opposed to single, isolated interventions, could record all of the objective measures that reflect “wellness”. If a CAM intervention improves several measurable indicators of “wellness”, it could be considered generally beneficial. For example, a study may demonstrate that a particular diet, food or dietary supplement may fail to confer a statistically significant reduction in blood pressure. The same intervention may have a modest impact on several other biomarkers of disease or “wellness”, which over time could significantly reduce the chance of a cardiovascular event or the development of chronic disease.

In addition, for clinical trials that utilize herbs, nutrients and other CAM interventions, CRN recommends NCCAM emphasize clinical trials involving subjects who are considered “at risk”, but not yet clinically diagnosed with a particular disease or condition. This allows for more cost effective demonstration of risk reduction, e.g. utilize subjects who are at risk for osteoarthritis to demonstrate the OA risk reduction effect of glucosamine and chondroitin sulfate. While CRN supports risk reductions research done on “at risk” individuals we are also in support of condition-based research that demonstrates the benefit of CAM therapies on individuals who already have a particular disease or condition.

In large clinical trials where diverse groups of individuals (wide ranges of ages, ethnicities, baseline diet and health, and both genders) make up the study population a significant benefit for a subset of this group may be missed. It is important to encourage NCCAM funded researchers of large clinical trials to perform sub-set analysis.

The strength of individual CAM therapies is often related to proper application of the therapy as part of a multi-component intervention. It is valuable for NCCAM resources to support clinical sites that utilize a particular complementary and/or alternative modality as “demonstration projects”. For example, a study could be designed to compare the safety, efficacy, and costs of a Chinese Medicine approach to a common medical condition as compared to a Standard Allopathic approach. Results from such comparisons may help inform consumers trying to choose how to approach their own personal health issues. CRN is aware that other CAM stakeholders will comment in greater depth on the use of demonstration projects for comparative effectiveness research and we voice our support for the allocation of resources as such projects.

## **Paper #2**

### **NCCAM Priority Setting — Framework and Other Considerations**

#### **1. The need for greater shaping of the Center's research portfolio**

CRN Comments:

CRN agrees it is important to focus investments of available resources on areas of research and development that offer the greatest potential of health benefit for the public or advancement of the general state of CAM research. It will also be important to continue directing some resources to a relatively broad, non-targeted, investigator-initiated, research project grant approach. The later approach casts a wide net, and continues to seed the research pipeline with new and emerging questions that can be built upon in the future.

CRN also feels that resources should be allocated to exploring the questions of research study design. The CAM research community needs clear criteria and guidelines for how best to study effects of nutrients and other naturally occurring bioactive compounds in humans, and subsequently how to evaluate those findings. Exploring the nutrient-chronic disease method using the same tools that were developed to explore the safety and efficacy of drugs has many inherent limitations.

NCCAM should be an integral part of high level discussions and investigations of whether it is appropriate to apply a drug-based research paradigm to assess nutrient and CAM-related questions. The former utilizes a reductionist approach and studies interventions in isolation. CAM, by definition combines multiple modalities using an integrative approach. Bringing together experts from both sides to explore this topic and possibly establishing alternatives to the drug paradigm is imperative to the future of CAM research.

**2. The four factors (scientific promise, extent and nature of practice and use, amenability to rigorous scientific investigation, and potential to change health or health care practices) identified as key components of a framework for research priorities.**

CRN Comments:

The four factors discussed in Paper #2 are rational guidelines for shaping priorities. CRN would like to emphasize that when considering option #3, "*amenability to rigorous scientific investigation*" the definition of rigorous scientific investigation should not be limited to reliance on the conventional randomized controlled trial (RCT) as the single gold standard. As mentioned in our previous comments, many experts opine that the misapplication of the drug-based research paradigm to assess nutrient and CAM interventions, may lead to incorrect conclusions.

Drugs trials are designed to study a substance that has a single targeted effect, is not homeostatically controlled by the body, and can be easily contrasted with a true placebo group. Drugs also act quickly and have a large and easily measurable effect. In contrast many nutrients and other CAM therapies that have multiple target sites, may be homeostatically controlled, and are not amenable to a true placebo group. In addition, for nutrients and bioactive compounds the effects may be subtle and may take decades to manifest.

In summary, CRN would like to see NCCAM display greater leadership in the investigation of new research methods designed to explore the complexities of CAM therapies and overcoming the methodological challenges presented by the very nature of these therapies.

**3. The types and sources of information that must be included in an optimal priority-setting process**

The NCCAM priority setting process should continue to rely heavily on stakeholder input. NCCAM should continue to seek expert input obtained through scientific workshops and forums; networking with investigators, practitioners, trade associations, consumers of CAM, and other stakeholders. The experience and viewpoints of top experts in the fields of nutrition, psychology, immunology, whole systems research, dietary supplements, Naturopathy, Chinese Medicine, Ayurvedic Medicine, Allopathic Medicine, Chiropractic Medicine, physical medicine, research design, and others are valuable assets the priority setting process.

In addition, when a proposed research project or program is related to a particular field, experts in the field should be consulted on the studies relevance and design. For example if a study is designed to investigate the safety and efficacy of a Traditional Chinese botanical, experts in the field of Chinese Medicine and botanical medicine should be consulted to see if the proposed project has plausibility.

### **Paper # 3:**

#### **Information and Communication About CAM Research and Decision making About CAM Use.**

##### **1. The major unmet needs of consumers and the general public in accessing, interpreting, and making use of research evidence about CAM**

CRN Comments:

When a consumer who lacks medical and scientific knowledge is faced with a medical condition they are interested in fair and balanced information about ALL of their health care choices. Consumers desire the ability to compare the potential benefits, risk, costs, resulting quality of life, and personal commitment that accompanies each choice.

Health care consumers have a wide variety of personal preferences and have grown frustrated with physicians who feel that, "*patient preference is least important*" as indicated by Tilbert and colleagues findings published in 2009 and referenced in Paper #3. Even if a specific CAM therapy is considered less efficacious than its pharmaceutical counterpart, some consumers may confidently choose the CAM therapy. Factors that may contribute to this decision include quality of life, personal or religious beliefs, cost and availability. NCCAM should place a greater emphasis on the accurate communication of information about CAM, in context with other health care options available to consumers.

To assist the general public make an informed choice about health care decisions it is imperative the public is aware of the impact a particular therapy will have on their quality of life. NCCAM may consider recommending that validated "quality of life" questionnaires be used in both CAM and Drug trials. In some cases, a drug trial may show superior efficacy that may be offset by side effects that result in a quality of life. The quality of life may be unacceptable to the consumer and result in non-compliance, which renders the CAM therapy superior in this context. When a consumer is choosing between using conventional drugs and/or CAM therapies, this information can be extremely valuable.

To be fair, the effectiveness of some CAM therapies may require a significant investment of time, money, and self-discipline by the patient. Consumers should also be made aware of the commitment required to achieve the established benefits of a particular therapy. For example, there are many diet and lifestyle approaches to treating chronic heart disease. If properly educated on the personal commitment required to achieve these results, some consumers may choose a pharmaceutical management to their condition.

Finally it is important that consumers are aware of what type of practitioner is qualified to administer a particular CAM therapy. Educating the general public regarding the training, licensing, and scope of practice of different CAM practitioners should be part of the NCCAM's outreach initiatives.

In summary, NCCAM communications should not be limited to the results of the latest clinical trials. This information should be placed in context with the real world and include information on the benefits, risks, costs, quality of life, and personal commitment that all of their choices (including allopathic and

CAM modalities) entail. In addition, when applicable, NCCAM communications should include the type of practitioner that is qualified to administer a particular therapy.

## **2. The major unmet needs of health care providers in accessing, interpreting, and making use of research evidence about CAM**

CRN Comments:

When interpreting and communicating research results to physicians, too often the message is black or white. The results of studies are communicated to health care providers in a fashion that suggests that a particular CAM therapy either works or does not work, when in reality it is much more complex.

Health care practitioners make treatment choices based on a wide variety of criteria. Often the inclusion or exclusion criteria for patients in a study make the results of that study not relevant to the patient sitting in their office. Health care practitioners would benefit from an evidentiary grading system that correlates different levels of evidence, with different levels of recommendation.

For example, study results that suggest a particular CAM therapy is safe and may help some individuals may be an appropriate level of evidence to support individual consumer choice. When results suggest a therapy is safe and that efficacy is probable, this level of evidence may be appropriate for individual physician recommendations. When results suggest a treatment is safe and efficacious, this level of evidence may support inclusion into physician treatment guidelines as deemed appropriate by experts in that particular field. The highest level of evidence of safety and efficacy can be appropriate for public health recommendations.

Developing a communication system that translates research results into different levels or grades of evidence that support different levels of confidence for practitioner recommendations broadens consumer and physician choices. A communication system that informs practitioners in such a fashion could also discourage over-reaching conclusions, such as “acupuncture does not work”, which sounds nonsensical to a fourth generation TCM practitioner whose experience suggests just the opposite or patient who has had their migraine headaches eliminated by an acupuncturist.

## **3. Research needed to better understand how both health care providers and the general public make decisions about CAM practice and use**

It is important for all health care providers to adopt a philosophy that seeks out therapies that are in the best interest of the individual patient, at a particular point in time. It would be helpful to better understand why health care practitioners tend to align with a particular philosophy and feel threatened by other modalities and philosophies.

Dogmatic opinions such as “herbs do not work” or “all pharmaceutical drugs are bad” are too dominant amongst all types of practitioners. It would be helpful to identify and gain a better understanding of unsubstantiated biases that are held by practitioners and how these biases may influence decision making about the use or avoidance of a particular modality. Understanding the source and influence of

biases may serve as valuable information that can assist in removing these biases, so that all stakeholders can make informed choices.