



Testimony
Before the Subcommittee on Human Rights and
Wellness
Committee on Government Reform
United States House of Representatives

Ongoing Research on Dietary
Supplements at the National
Institutes of Health

Statement of

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Mr. Chairman and Members,

Thank you for the opportunity to appear before you today representing the Office of Dietary Supplements (ODS) at the National Institutes of Health (NIH). I became Director of ODS in late 1999, and I had the pleasure of appearing before the Committee two years ago, in July 2002. At that time, I provided you with some details about the activities of ODS and highlighted both the opportunities and the challenges associated with developing good science in the field of dietary supplements.

Prior to highlighting ODS and other NIH efforts related to five supplement ingredients that you identified – folate, calcium, omega-3 fatty acids, glucosamine, and saw palmetto – I want to give you a brief update of our continuing and emerging collaborative investigations of dietary supplements, particularly as they relate to reducing the risk of chronic diseases.

Health Effects of Dietary Supplement Ingredients

Dietary supplements are widely used by American consumers, often in combination with other lifestyle measures such as diet and physical activity, for their potential benefits in health promotion and disease prevention. Surveys, such as the National Health and Nutrition Examination Survey (NHANES), which is conducted by the Centers for Disease Control and Prevention (CDC) and funded in part by NIH organizations including ODS, show that 50% or more of American adults use supplements on a regular basis, primarily vitamins and minerals, but herbal and other supplements as well¹. There are many hopes pinned on dietary supplements for the improvement of health and prevention of disease, hopes that have been realized when some of them have been put to modern scientific testing. Examples of these include:

- Folic acid to reduce the risk of neural tube defects, one of the most common birth defects. As a result of this research, the CDC and other partners in the National Folic Acid Campaign aim to educate all women of childbearing age to consume 400 micrograms of synthetic folic acid daily from vitamin supplements and/or fortified foods in addition to eating food folate in a healthful diet;
- Calcium to reduce the risk of osteoporosis. The NIH Consensus Development Conference in 1997 concluded that while the preferred source of calcium is through calcium-rich foods, both calcium supplements and calcium-fortified foods are other means by which optimal calcium intake can be reached for those who cannot meet this need by eating conventional foods;
- Iron supplementation during pregnancy to prevent maternal anemia and delivery of premature infants;
- Vitamin B-12 supplementation for those (particularly among the elderly) who cannot readily absorb food-bound vitamin B-12;
- Vitamin and antioxidant supplementation to prevent progression of macular degeneration; and

¹ Radimer K, Bindewald B, Hughes J, Irvin B, Swanson C, Picciano MF: Dietary supplement use by US adults: Data from the National health and Nutrition Examination Survey, 1999-2000. Amer J Epidemiol 160:339-349, 2004.

- Supplements promoting antioxidant activity generally to reduce the risk of oxidative damage from exposure to environmental agents.

Of the approximately 30,000 dietary supplements on the market in the United States, there are many that have not undergone the rigorous scientific testing needed to establish their efficacy and safety. Some are under active investigation at the NIH, including:

- Ginkgo biloba: does it prevent decline of cognitive function in older individuals?
- Dietary phytoestrogens: do they prevent bone loss in postmenopausal women?
- Selenium and vitamin E: alone or in combination, do they prevent prostate cancer?; and
- Glucosamine and chondroitin: alone or in combination, do they diminish the pain associated with knee osteoarthritis?

Other dietary supplements have been shown to be potentially harmful to some individuals; for example, research has shown that beta-carotene, instead of reducing cancer risk, may actually increase lung cancer incidence among cigarette smokers. For still others, there are signals of concern (e.g., from adverse event reports) that need to be followed up in a scientifically sound manner.

The Expanding Role of ODS in Dietary Supplement Research

ODS was mandated by the Dietary Supplement Health and Education Act of 1994 (DSHEA) and was formally installed in the Office of the Director of NIH in 1995. Its mission, based on a comprehensive strategic planning process, is to “identify and foster research on the health benefits and risks of these substances based on the merit of the underlying scientific evidence.”

Last year, ODS re-evaluated its Strategic Plan with input from a wide range of stakeholders. I am pleased to announce that this Plan has just been published and that it can be found on the ODS website (<http://ods.od.nih.gov>). The Strategic Planning process helped us considerably in assessing how far we had come in the past five years and in guiding ODS activities for the future. ODS has been able to embark on a number of important activities, including:

- Co-funding of dietary supplement research grants with other Institutes and Centers (ICs) at NIH. In FY 2004, ODS has been able to co-fund 90 grants with 15 NIH ICs for a total investment of approximately \$15 million;
- Sponsoring conferences and workshops, again most often in collaboration with other ICs; since the inception of this program, ODS has sponsored nearly 100 such events;
- Developing a series of fact sheets on vitamins and minerals, in collaboration with the NIH Clinical Center;
- Initiating two important database efforts: the *International Bibliographic Information on Dietary Supplements (IBIDS)*, developed jointly with the National Agricultural Library of the U.S. Department of Agriculture (USDA), which cites roughly 750,000 references to the world’s literature, and *Computer Access to Research on Dietary Supplements (CARDS)* to track the Federal investment in

dietary supplement research. The current CARDS data set describes the NIH investment from FY 1999 to FY 2003; over that period of time, NIH alone has invested over \$770 million in supporting nearly 2600 research projects related to dietary supplements; and

- An especially important activity of ODS is its program of comprehensive Dietary Supplement Research Centers around the country. There are six of these multidisciplinary Centers (located at Purdue University/University of Alabama at Birmingham, Iowa State University/University of Iowa, University of Illinois at Chicago, University of California at Los Angeles, University of Arizona, and University of Missouri/Missouri Botanical Garden) whose primary focus is botanical dietary supplements. The Centers are jointly funded with the National Center for Complementary and Alternative Medicine (NCCAM) and the National Institute of Environmental Health Sciences (NIEHS); other NIH components, including the National Institute of General Medical Sciences (NIGMS) and the Office of Research on Women's Health (ORWH), also participate in funding these Centers.

More recently, the budget for ODS has grown, from \$3.5 million in FY 1999 to \$26 million in FY 2004. This has permitted expansion of our research, education, and communications agenda into new and important areas:

- Evidence-based reviews of dietary supplement efficacy and safety, in collaboration with other NIH ICs and the Agency for Healthcare Research and Quality (AHRQ). (I will return to this activity later in my testimony.);
- Surveys of dietary supplement use, e.g., the NHANES conducted by the CDC;
- Development of a database of dietary supplement ingredients in collaboration with the USDA;
- Development, validation, and dissemination of analytical methods and reference materials for dietary supplements, in collaboration with the Food and Drug Administration (FDA) and a number of private sector organizations²;
- Development of a formal program related to the role of dietary supplements in health promotion and reduction of risk for chronic diseases;
- Expansion of our information and communications program;
- Expansion of training and career development activities; and
- Participation in international research efforts.

In partnership with other NIH ICs, ODS funds research grants in areas such as:

- Folate-genome interactions in colorectal cancer;
- Zinc nutrition and brain development in Southern Ethiopia;
- Mechanisms of prostate cancer prevention by lycopene;
- Aging, vitamin E, and immune function;
- Chromium picolinate in the metabolic syndrome;
- Mitochondrial rRNA methylation and effects of ethanol and S-Adenosyl-L-Methionine (SAME);

² Saldanha LG, Betz JM, Coates PM: Development of the analytical methods and reference materials program for dietary supplements at the National Institutes of Health. *J AOAC Int.* 87:162-165, 2004.

- Neuromodulatory effects of ginkgolides and bilobalides;
- Conjugated linoleic acid effects on lipid synthesis;
- Whether high dose B vitamins delay age-related decay; and
- The role of St. John's Wort in the management of minor depression.

ODS sponsors workshops and conferences, again in collaboration with other organizations both within and outside NIH. These meetings are valuable sources of information in assisting us to shape upcoming research activities. Some recent and upcoming conferences include:

- The Role of SAME in Treatment of Alcoholic Liver Disease. This led to issuing a Request for Applications (RFA) in 2002 with the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and NCCAM; these 3 organizations jointly funded eight grants from this RFA;
- Diet, DNA Methylation Processes and Health, sponsored by the National Cancer Institute (NCI) with participation by ODS, NIEHS, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Child Health and Human Development (NICHD), and the FDA. This led to release of an RFA jointly sponsored by NCI and ODS and eventual funding of 10 grants;
- Three conferences on Dietary Supplement Use in Children, in Women, and in the Elderly (with NICHD, NCCAM, NIA, ORWH and others);
- Vitamin D and Health in the 21st Century, jointly sponsored by ODS and NICHD; and
- An NIH State-of-the-Science Conference on the Role of Multivitamins/multiminerals in Chronic Disease Prevention, to be organized by the NIH Office of Medical Applications of Research with sponsorship from ODS and many other NIH ICs.

The development of other new areas of investigation relies on forging strategic partnerships with other agencies as well. A few current examples include Interagency Agreements with:

- The National Center for Health Statistics at CDC, to support improvements in the ability of NHANES to more accurately assess dietary supplement intake in the U.S., as well as biomarkers of supplement usage related to health outcomes;
- AHRQ, to develop evidence reports of dietary supplement efficacy and safety. The first of these, on ephedra efficacy and safety in weight management and athletic performance enhancement, was published in early 2003³; others have been completed (a series on the health effects of omega-3 fatty acids) or are underway on topics that include "Vitamin D Adequacy and Health" and

³ Shekelle PG, Hardy ML, Morton SC et al: Efficacy and safety of ephedra and ephedrine for weight loss and athletic performance: a meta-analysis. JAMA 289:1537-1545, 2003.

“Relationship between Antioxidants in Berries and B Vitamins and Age-related Neurodegenerative Disorders”;

- FDA, to support the development and validation of analytical methods by the Association of Official Analytical Chemists (AOAC) International; and
- The National Institute of Standards and Technology (NIST) in the Department of Commerce, to support development of standard reference materials.

We have worked with partners in the private sector in a number of areas:

- Publication of an annual bibliography of outstanding research in dietary supplements, initially with the Consumer Healthcare Products Association. This effort, now fully under the auspices of ODS, is in its fifth year;
- Publication of “Botanical Pharmacognosy and the Microscopic Characterization of Botanical Raw Materials” by the American Herbal Products Association was supported in part by ODS;
- Publication of a summary of the conference “Dietary Supplement Use in the Elderly” in collaboration with the Foundation for the National Institutes of Health and Virgo Publishing Inc.;
- Publication of "What Supplements Are You Taking? Does Your Healthcare Team Know? It Matters and Here is Why", a brochure for the elderly, jointly produced by FDA and ODS in collaboration with a number of private sector organizations;
- Regular participation of ODS staff in educational and scientific sessions at industry meetings and expositions; and
- A crucial effort is engaging with industry – as well as other federal agencies, non-governmental organizations and academia – to develop, validate, and disseminate analytical methods and reference materials for dietary supplements.

I would like to stress a theme that runs through all of the activities that I have mentioned: all were developed in collaboration with other organizations, both within and outside the NIH. They could not have been accomplished otherwise. In my view, these collaborations are crucial to the advancement of science and dissemination of information in the area of dietary supplements. Further details of these and other interactions can be found on the ODS website (<http://ods.od.nih.gov>).

Let me now turn to the five supplement ingredients that you have identified as being of particular interest: folate, calcium, omega-3 fatty acids, glucosamine, and saw palmetto. I indicated earlier that the Federal investment in dietary supplement research has been extensive over the last five years. While the data are still being analyzed, I can tell you that, taken together, research on these five ingredients has accounted for roughly one-quarter of that investment. While much of the funding has been directed to basic research, increasing attention has been paid to conducting appropriate human studies. Some examples include:

Glucosamine

A clinical trial of glucosamine and chondroitin sulfate for knee osteoarthritis (Glucosamine/Chondroitin Arthritis Intervention Trial or GAIT), jointly sponsored by

NCCAM and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), has met its recruitment goals and is due to be completed within a year.

Saw palmetto

A clinical trial of saw palmetto and *Pygeum africanum* for urinary symptoms in men (Complementary and Alternative Medicine for Urinary Symptoms, or CAMUS) was recently funded by NIDDK, NCCAM, and ODS.

Omega-3 fatty acids

As part of its program of evidence-based reviews of dietary supplement efficacy and safety, ODS sponsored a series of AHRQ-contracted evidence reports of the health effects of omega-3 fatty acids for a number of conditions. Several of these have been published this year – on cardiovascular disease (CVD), asthma, and type 2 diabetes, among others – and several more will appear early in 2005. The evidence report on CVD concluded that there was substantial and strong evidence for a benefit of omega-3 fatty acids in the secondary prevention of CVD, but that there was considerably less evidence for an effect on primary prevention. Thus, while strong clues were obtained about the positive health effects of omega-3 fatty acids on the future risk of disease in people with existing CVD, the same cannot yet be said for the general population. As a result of this report⁴, NHLBI and ODS convened a working group earlier this year to assess future research needs related to primary and secondary prevention in this area; the working group made recommendations for clinical trials necessary to answer important outstanding questions about omega-3 fatty acids⁵. These recommendations are currently being pursued.

Calcium

NIH funds considerable clinical research related to calcium. One intramural NICHD study that I would like to draw to your attention is the trial of Supplemental Calcium in Overweight People, which examines the health effects of calcium supplements in overweight adults. In addition, ODS has recently published a Fact Sheet on Calcium to inform consumers about the health benefits of adequate calcium intake⁶. All Fact Sheets that ODS issues are regularly reviewed and updated as necessary to reflect important advances in science.

Folate

Finally, based on results of the recently available NHANES data on folate and vitamin B-12, along with developments in methodology for their assessment, ODS is working with colleagues at NIH and other Federal agencies in evaluating the measures that are employed to determine health outcomes from intake of folate and vitamin B-12. There is particular interest in the elderly, in whom intake of these vitamins has been implicated in cognitive functioning and cardiovascular health.

⁴ <http://www.ahrq.gov/clinic/tp/o3cardtp.htm>

⁵ <http://www.nhlbi.nih.gov/meetings/workshops/omega3-summary.htm>

⁶ <http://ods.od.nih.gov/factsheets/calcium.asp>

Closing Remarks

Mr. Chairman and Members of the Committee, I thank you again for inviting me to review the accomplishments of the Office of Dietary Supplements at NIH, and to highlight some of its ongoing research opportunities and challenges. I would be happy to answer your questions.