Testimony
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United States House of Representatives

The Mission and Work of the Office 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 at this hearing "The Regulation of Dietary Supplements: A Review of Consumer Safeguards", representing the Office of Dietary Supplements (ODS) at the National Institutes of Health (NIH). I became Director of ODS in late 1999, and I have had the pleasure of appearing before the Committee twice before, in July 2002 and September 2004. At those visits, I provided you with some details about ongoing activities of ODS and other NIH Institutes and Centers (ICs) and I highlighted both the opportunities and the challenges that NIH faces as it develops a solid scientific base in the field of dietary supplements.

You have asked me today to address the work and mission of ODS, how we partner with other agencies and organizations, including the Food and Drug Administration (FDA), to meet common goals, and how we work to educate the public regarding dietary supplements. These are all very important matters, ones that occupy me and my staff every day. I will also use this opportunity to tell you about the broader NIH involvement in dietary supplement research. While ODS portrays itself as a catalyst in stimulating trans-NIH research activities in this area, the NIH ICs, as you will see, have had a longstanding commitment to research in this field.

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. At a hearing of this Committee in 2004, I

commented that population 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 well[1].

There are many hopes pinned on dietary supplements for improving health and reducing the risk of chronic disease, hopes realized when in some cases by modern scientific testing. Examples of these include:

- Folic acid to reduce the risk of neural tube defects, one of the most common birth defects;
- Iron supplementation during pregnancy to reduce the risk of maternal anemia;
- Vitamin B-12 supplementation for those (particularly among persons over 50) who cannot readily absorb food-bound vitamin B-12;
- Vitamin and antioxidant supplementation to reduce the rate of progression of macular degeneration; and
- Use of vitamin D supplements by older adults and people exposed to insufficient sunlight to ensure adequate vitamin D status for optimal calcium absorption and reduced risk of bone loss.

With NIH support for dietary supplement research, much already has been accomplished. For example, preliminary results of a National Center for Complementary and Alternative

[1] Radimer K, Bindewald B, Hughes J, Irvin B, Swanson C, Picciano MF: Dietary supplement use by US

Medicine (NCCAM)- and National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)-funded trial recently were published in the *New England Journal of Medicine* that suggest that the popular dietary supplements, glucosamine and chondroitin sulfate, may provide pain relief to patients with moderate-to-severe pain from knee osteoarthritis. Also, ODS, NCCAM, and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) are partnering to learn more about the potential of milk thistle to address chronic liver disease. In addition, there are ongoing clinical trials of dietary supplement ingredients funded by several components of the NIH. Examples include the National Cancer Institute (NCI)-funded SELECT trial to investigate the role of vitamin E and selenium in preventing prostate cancer, and a trial funded by several NIH Institutes and Centers (ICs) (NCCAM, ODS, and the National Institute on Aging – NIA) to explore whether the dietary supplement Ginkgo biloba can prevent or forestall the neurodegenerative changes associated with Alzheimer's disease.

On the other hand, ingredients used in some dietary supplements on the market in the United States have not undergone the rigorous scientific testing needed to establish their efficacy and safety; some of these have been evaluated by NIH ICs or are under active early investigation. Other ingredients contained in some dietary supplements have been shown to be potentially harmful to some individuals; for example, research has shown that beta-carotene, instead of reducing lung cancer risk, may actually increase it among cigarette smokers. For still others, there are signals of concern (e.g., such as herb-drug

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adults: Data from the National health and Nutrition Examination Survey, 1999-2000. Amer J Epidemiol 160:339-349, 2004.

interactions and adverse event reports, such as those shown for ephedra-containing dietary supplements) that need to be addressed in a scientifically sound manner.

The Work and Mission of the Office of Dietary Supplements

ODS was mandated by the Dietary Supplement Health and Education Act of 1994 (DSHEA). It was formally installed in the Office of the Director of NIH in 1995, and so we have just celebrated our tenth anniversary. Its mission is to "strengthen knowledge and understanding of dietary supplements by evaluating scientific information, stimulating and supporting research, disseminating research results, and educating the public to foster an enhanced quality of life and health for the U.S. population".

ODS has in place its second 5-year Strategic Plan which was developed with input from a wide range of stakeholders. This Plan has been published and 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 since the first plan was published in 1998 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 2005, ODS invested approximately $15 million in co-funding 100 grants with 15 NIH ICs.
- Sponsoring conferences and workshops, again most often in collaboration with other ICs; since the inception of this program, ODS has sponsored more than 100

such events. These are open to the public and summaries are available on the ODS Web site.

- Developing a series of fact sheets on dietary supplements, in collaboration with NCCAM and the NIH Clinical Center.
- Initiating two important publicly accessible Web-based databases: 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 2004; over that period of time, NIH alone has invested over $1 billion in supporting more than 3500 research projects related to dietary supplements.
- An especially important activity of ODS, in collaboration with NCCAM and the National Institute of Environmental Health Sciences (NIEHS), is its program of comprehensive Dietary Supplement Research Centers located in academic settings 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; Pennington Biomedical Research Center; Memorial Sloan Kettering Cancer Center; and Wake Forest University) whose primary focus is interdisciplinary research on botanical dietary supplements.

The budget for ODS has grown, from $3.5 million in FY 1999 to approximately $27 million in FY 2006. 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.
- Nationally representative surveys of dietary supplement use over time, e.g., the NHANES conducted by the Centers for Disease Control and Prevention (CDC). ODS contributes to this effort in several ways and is developing an accurate, easy-to-use, Web-based analysis tool to determine nutrient intakes from foods and supplements by various population groups.
- Development of a database of dietary supplement ingredients in collaboration with the U.S. Department of Agriculture (USDA); this is essential information for evaluating intakes from dietary supplements for the U.S. population and for monitoring intakes over time; it will provide much-needed information for the research community in designing and monitoring studies; when completed, it will also be useful for the industry and for consumers to have ready availability to information on the composition of a broad range of marketed dietary supplement products.
- Development, validation, and dissemination of analytical methods and reference materials for dietary supplements, in collaboration with FDA and a number of private sector organizations[2], including the Association of Official Analytical

[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.

Chemists (AOAC) International. This will be especially useful for researchers and industry users. AOAC International has also developed training activities for the industry and research communities as part of this program.

- Expansion of our information and communications program following a comprehensive evaluation and assessment.

In partnership with other NIH ICs, ODS funds research grants in areas such as (primary IC in parentheses):

- Alpha-tocopherol modulation of xenobiotic metabolism (NIDDK);
- Black cohosh and menopause-related anxiety (NCCAM);
- Phytoestrogens and aging: dose, timing, and tissue (NIA);
- Vitamin D and progression of knee osteoarthritis (NIAMS);
- Aging, vitamin E, and immune function (NIA);
- Chromium enhancement of insulin signaling (NCCAM);
- Mechanisms of alcohol-induced immunosuppression (National Institute on Alcohol Abuse and Alcoholism – NIAAA);
- Folate-genome interactions in colorectal cancer (NCI);
- Neuromodulatory effects of ginkgolides and bilobalides (National Institute of Mental Health);
- Modulation of autoimmunity by green tea polyphenols (NCCAM):
- Cranberry effects on Candida albicans adherence (NCCAM);
- Mechanisms of prostate cancer prevention by lycopene (NCI).

ODS sponsors workshops and conferences, again in collaboration with other organizations both within and outside NIH. These public meetings are valuable sources of information in assisting us to shape upcoming research activities. The outcomes of these conferences are summarized and available on the ODS Web site and are also often published in scientific journals. Some recent and upcoming conferences include:

- Diet, DNA Methylation Processes and Health, sponsored by NCI with participation by ODS, NIEHS, 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 the funding of 10 grants by NCI and ODS.
- Three conferences on Dietary Supplement Use in Children, in Women, and in the Elderly (with NICHD, NCCAM, NIA, the NIH Office of Research on Women's Health, and others).
- Biomarkers for Diet/Cancer Relationships, jointly sponsored by FDA, NCI, and ODS.
- Animal Diets for Use in Studying Phytoestrogen Effects, jointly sponsored by NIEHS and ODS.
- Vitamin D and Health in the 21st Century, jointly sponsored by ODS and NICHD.
- An NIH State-of-the-Science Conference on the Role of Multivitamins/ multiminerals in Chronic Disease Prevention, to be held in May 2006 and organized by the NIH Office of Medical Applications of Research with sponsorship from ODS and many other NIH ICs.

ODS Collaboration with Other Agencies and Organizations

The development of 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 (NCHS) 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 2003[3]. Other reports 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 "Relationship between Antioxidants in Berries and B Vitamins and Age-related Neurodegenerative Disorders". A complete list of these is available on the ODS Web site at the URL given at the end of this testimony. In all of these cases, the goal of the reports is to give ODS and its NIH partners an objective and independent view of the current state of the science as we make decisions about further research priorities.

[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.

- FDA, to support the development and validation of analytical methods by AOAC International.
- FDA and the National Institute of Standards and Technology (NIST) in the Department of Commerce, to support development of standard reference materials.
- Numerous agencies of the USDA, the Department of Health and Human Services (DHHS), and the Department of Defense (DoD) to identify and enhance research in support of the development of Dietary Reference Intakes.
- NIEHS and the Food and Agriculture Organization/World Health Organization (FAO/WHO) to support development of an international conceptual model for nutrient risk assessment.

Broader NIH collaborations with other agencies in pursuit of these goals are also important. Let me provide two examples:

- Several components of NIH (including ODS, NCCAM, NIAMS, and the National Institute on Drug Abuse – NIDA) joined FDA and the Drug Enforcement Administration (DEA) to fund the development of an animal model to evaluate the anabolic potential of steroids and steroid precursors, some of which are purported to be in dietary supplements.
- The National Toxicology Program (NTP), housed in NIEHS, is a joint activity with FDA's National Center for Toxicological Research (NCTR). The NTP is currently evaluating *Citrus aurantium*, an herb which has become popular in weight-loss products as a replacement for *Ephedra*, in standard animal toxicity and physiological models.

ODS has worked with partners outside of the government 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 sixth year.
- Publication of “Botanical Pharmacognosy and the Microscopic Characterization of Botanical Raw Materials” by the American Herbal Products Association, supported in part by ODS.
- Publication of a summary (one for health professionals, one for dietary supplement industry readers) 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 Health Care Provider Know? It Matters and Here’s Why", a brochure for the elderly, jointly produced by FDA and ODS in collaboration with a number of private sector organizations.
- Collaboration with the National Consumers League on the topic of dietary supplements and anticoagulant therapies.
- Regular participation of ODS staff in educational and scientific sessions at academic meetings, consumer conferences, industry meetings, and expositions.
- Engaging with federal agencies such as the FDA, industry, 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 here. All were developed as the result of collaborations with other organizations at NIH, in other agencies of DHHS, and in other government departments. They could not have been accomplished otherwise. These collaborations enriched our program in many ways, including the sharing of scientific expertise, leveraging of limited resources, and the ability to reach a broader and more diverse group of stakeholders and audiences. In my view, this is crucial to the advancement of science and dissemination of information in the area of dietary supplements. From these collaborations, we know that there is a critical need for additional research on dietary supplements, particularly botanical products. To discover the full potential of dietary supplements for the public health, more must be learned about their safety and efficacy through basic and clinical research, product standardization, and improved research design. Further details of these and other interactions can be found on the ODS Web site (http://ods.od.nih.gov).

Public Education Efforts

At the end of the day, a major goal of our work is to improve the information available to consumers as they make healthcare choices. ODS employs a number of strategies to make information available to the public. Some of them have already been mentioned. Many of these resources are available on the ODS Web site and are listed below.

- Complete List of Dietary Supplement Fact Sheets and Related Information

http://ods.od.nih.gov/Health_Information/Information_About_Individual_Dietary_Supplements.aspx

- Dietary Supplements: Background Information (fact sheet)
  http://ods.od.nih.gov/factsheets/dietarysupplements.asp
- What Supplements Are You Taking?
  http://ods.od.nih.gov/pubs/partnersbrochure.asp
- Annual Bibliographies of Significant Advances in Dietary Supplements
  http://ods.od.nih.gov/Research/Annual_Bibliographies.aspx
- CARDS (Computer Access to Research on Dietary Supplements Database)
  http://ods.od.nih.gov/Research/CARDS_Database.aspx
- IBIDS (International Bibliographic Information on Dietary Supplements Database)
  http://ods.od.nih.gov/Health_Information/IBIDS.aspx
- Complete List of ODS-Sponsored Evidence Reports on Dietary Supplement Efficacy and Safety
  http://ods.od.nih.gov/Research/Evidence-Based_Review_Program.aspx#reportsinprogress

Summing Up

Mr. Chairman and Members of the Committee, I thank you again for inviting me to talk with you about the role that the Office of Dietary Supplements at NIH plays and to

highlight some of its ongoing research and education efforts. I would be happy to answer your questions.