A Report to the Public

Office of Dietary Supplements
Office of Disease Prevention
National Institutes of Health
U.S. Department of Health and Human Services

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Introduction

The *mission* of the Office of Dietary Supplements (ODS) of the National Institutes of Health (NIH) 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 is now more than 10 years old and is developing a strategic plan for 2010–2014. The Office's previous strategic plans have guided its activities and this report discusses some of the results of those activities.

This report has three parts:

1. Comments from the Director of ODS.
2. A review of ODS and its activities from 2004 to the present, as well as in the future.
3. A detailed report on the program activities through which ODS accomplishes it mission.

Please read this report and share your responses to the following questions:

- Are the current strategic goals adequate?
- Is ODS meeting its stakeholders' needs?
- In the future, should some of ODS's current programs or activities be given higher (or lower) priority?
- How can ODS more effectively provide useful information to the ODS user community, including consumers, investigators, practitioners, industry, media, policy makers, government, and other interested parties?

Ways to send in comments and questions:

- Send an e-mail to ODS: ODSPlan@od.nih.gov
- Contact ODS through its Strategic Plan Web site: http://ods.od.nih.gov/strategicplan
- ODS town meeting webinars: ODS will hold a series of four webinars at the times and topics listed below to hear comments on and suggestions for ODS initiatives for possible inclusion in the 2010-2014 ODS Strategic Plan. The topic is taken from the four areas described in this background paper, *A Report to the Public*. Each webinar will begin with brief comments by a Federal partner and a stakeholder on the topic of that webinar. The remainder of each webinar will be devoted to hearing public comments. You should register in advance to make an oral comment of up to three minutes (see ODS Web site above

  Research Support: Thursday, January 29, 2009, 1:00–2:00 pm EST
  Research Tools: Tuesday, February 3, 2:00–3:00 pm EST
  Science-Policy Interactions: Wednesday, February 11, 1:00–2:00 pm EST

Communications: Thursday, February 19, 2009, 2:00–3:00 pm EST

If you would like to participate in one or more of these webinars, register through the ODS Strategic Plan Web site: http://ods.od.nih.gov/strategicplan.

Note: All webinars will be archived on the ODS strategic plan Web site. So even if you cannot participate during the times listed above, you can view the session and submit comments or questions at a later time.

Part 1: Comments from the Director, Office of Dietary Supplements

The Office of Dietary Supplements (ODS) is a highly visible Office within the National Institutes of Health (NIH). Over the years, ODS has been the focus of considerable interest from many stakeholders. From time to time, it is fitting for the Office to submit itself to public scrutiny to share the remarkable outcomes of ODS investments and provide an opportunity for input into its future plans.

As ODS considers revisions to its current strategic plan, two issues stand out:

- The ODS budget probably will not grow significantly, if at all; thus, setting priorities and critically evaluating the output and the future of every ODS program are of paramount importance.
- ODS implements its goals through collaboration; to do that effectively, it needs to continue building its communication and outreach activities with various stakeholder communities.

Priority Setting and Evaluation. The budget for ODS (and, indeed, for all of NIH) has remained essentially unchanged since 2004, when the NIH budget stopped doubling. The appropriation is still a generous one and it continues to allow for the advancement of science in dietary supplements. This strategic planning period will permit a critical assessment of ODS's investments and what they have yielded. ODS needs and welcomes input from others to inform its decisions about future investments.

Building Communities. ODS is committed to promoting good science to inform public health policy and to help consumers make knowledgeable decisions about their own health care. To promote good science, ODS has partnered with research communities—academic, government, and industry—to promote development of the knowledge base for dietary supplements. These partnerships are detailed in this report.

It is truly gratifying that for every dollar that ODS invested in research related to dietary supplements in 2007, NIH invested $17. This shows that NIH has been and continues to be committed to funding the best science on the health effects of dietary supplement ingredients.

Because the science of dietary supplements has a broad impact, ODS has also taken a leadership role in spearheading a number of research initiatives that extend beyond NIH. These initiatives include the evidence-based reviews on omega-3 fatty acids, soy, and vitamin D, together with their attendant Federal working groups. ODS also convened the Federal Dietary Supplement Working Group, which shares ideas and identifies initiatives to advance dietary supplement research. These initiatives and the working group include members from other agencies in the Department of Health and Human Services (DHHS), such as the Food and Drug Administration (FDA), Agency for Health Research and Quality (AHRQ), and Centers for Disease Control and Prevention (CDC), as well as agencies from the U.S. Department of Agriculture (USDA), Department of Commerce, and Department of Defense (DoD). Building bridges across government components has been very important to ODS in gathering input on and building partnerships to address emerging scientific issues related to dietary supplements.

In addition to representatives of a broad range of government agencies, industry-based researchers have informed ODS analytical methodology priorities through national meetings and workshops and have shared and collaborated in validating analytical tools. These interactions have contributed substantially to developing and disseminating the analytical tools and methods that are so essential for advancing the science of dietary supplements.

Enhancing communications. The effort to expand ODS communications and outreach activities has already paid off handsomely: ODS is able to respond rapidly and effectively to consumer and media inquiries; ODS staff are regularly called on to comment on new and emerging research; lines of communication are well coordinated; and the communications tools that ODS uses (Web site, fact sheets, exhibits at conferences, pamphlets) are valuable and current. These developments are an outcome of the evaluation of the ODS communications program in 2005 and are the basis for future improvements in communications and outreach.

Because ODS activities to stimulate and enhance dietary supplement research have implications for policy—such as nutrient intake recommendations and, by extension, national dietary guidance—ODS staff need to ensure that science is effectively translated into public policy. Therefore, outreach efforts by ODS include the policy community as well.

This report describes what ODS is currently doing to meet its legislative mandates and to enhance the health of the public. ODS invites review and comment from its stakeholders and other interested parties as part of the process for developing a strategic plan for 2010–2014.

Paul M. Coates, Ph.D.
Director, Office of Dietary Supplements in the Office of Disease Prevention, Office of the Director, NIH, DHHS

Part 2: A Review of ODS and Its Activities

Background

The Office of Dietary Supplements (ODS) was created in 1995 in the Office of Disease Prevention, Office of the Director, National Institutes of Health (NIH), to meet the requirements of the Dietary Supplement Health and Education Act (DSHEA) of 1994. The DSHEA defined the purposes and responsibilities of ODS as follows:

Purposes:

- *To explore more fully the potential role of dietary supplements as a significant part of the efforts of the United States to improve health care.*
- *To promote scientific study of the benefits of dietary supplements in maintaining health and preventing chronic disease and other health-related conditions.*

Responsibilities:

- *To conduct and coordinate scientific research within NIH relating to dietary supplements and the extent to which the use of dietary supplements can limit or reduce the risk of diseases.*
- *To collect and compile the results of scientific research relating to dietary supplements, including scientific data from foreign sources.*
- *To serve as the principal advisor to the Secretary and to the Assistant Secretary for Health and provide advice to the Director of NIH, the Director of the Centers for Disease Control and Prevention, and the Commissioner of the Food and Drug Administration on issues relating to dietary supplements. These issues include dietary intake regulations, the safety of dietary supplements, the claims characterizing the relationship between the use of dietary supplements and the prevention of disease or other health conditions and the maintenance of health, and scientific issues arising in connections with the labeling and composition of dietary supplements.*
- *Compile a database of scientific research on dietary supplements and individual nutrients.*
- *Coordinate funding relating to dietary supplements for the NIH.*

Subsequent congressional mandates directed ODS to develop a botanical research center initiative (1999), conduct evidence-based reviews of the efficacy and safety of dietary supplements (2001), and accelerate the validation of analytic methods and reference materials for dietary supplements (2004).

Definition of "Dietary Supplement"

The DSHEA established a formal definition of "dietary supplement" using several criteria.[1] By law, a dietary supplement is a product taken by mouth that contains a dietary ingredient: vitamins, minerals, amino acids, and herbs or botanicals, as well as other substances that can be used to supplement the diet.

In defining a dietary supplement, the DSHEA allowed various types of statements on the label of dietary supplements, although claims may not be made about the use of a dietary supplement to diagnose, prevent, mitigate, treat, or cure a specific disease unless approved under the new drug provisions of the Federal Food, Drug and Cosmetics Act.

The ODS Mission Statement

ODS developed its mission statement as part of its first strategic planning process in 1998:

> *The **mission** of ODS 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 Strategic Planning

ODS has used strategic planning to establish and review the goals that drive its activities since its establishment in 1995. The Office's first strategic planning process included discussions with NIH Institute and Center (IC) directors and with representatives of the scientific community, industry, other Federal government agencies, and the public to identify areas of common interest.

The current ODS director, Paul M. Coates, Ph.D., led the planning process for the 2004–2009 strategic plan, *Promoting Quality Science in Dietary Supplement Research, Education, and Communication.* Dr. Coates is also leading the development of the strategic plan for 2010–2014.

The 2004–2009 ODS strategic plan included the five goals developed in the 1998 strategic plan, but ODS updated the statements and initiatives for each goal.[2] These goals were guided by mandates set forth by the 103rd Congress in the DSHEA for ODS. These strategic goals focused on research, communication, and education, with research as the major component in four of the five goals. ODS's five strategic goals were to:

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[1] DSHEA states: A dietary supplement is (i) a product (other than tobacco) that is intended to supplement the diet that bears or contains one or more of the following dietary ingredients: a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients; (ii) intended for ingestion in pill, capsule, tablet, or liquid form; (iii) not represented for use as a conventional food or as the sole item of a meal or diet; (iv) labeled as a dietary supplement; and includes products such as an approved new drug, certified antibiotic, or licensed biologic that was marketed as a dietary supplement or food before approval, certification, or license (unless the Secretary of Health and Human Services waives this provision).

[2] See Appendix A for the complete list of goals and initiatives in the 2004 – 2009 Strategic Plan. The complete Strategic Plan may be found at: http://ods.od.nih.gov/strategicplan2004

1. Expand the evaluation of the role of dietary supplements in disease prevention and in reduction of risk factors associated with disease.

2. Foster research that evaluates the role of dietary supplements in maintaining and improving optimal physical and mental health and performance.

3. Stimulate and support research to further understanding of the biochemical and cellular effects of dietary supplements on biological systems and their physiological impact across the life cycle.

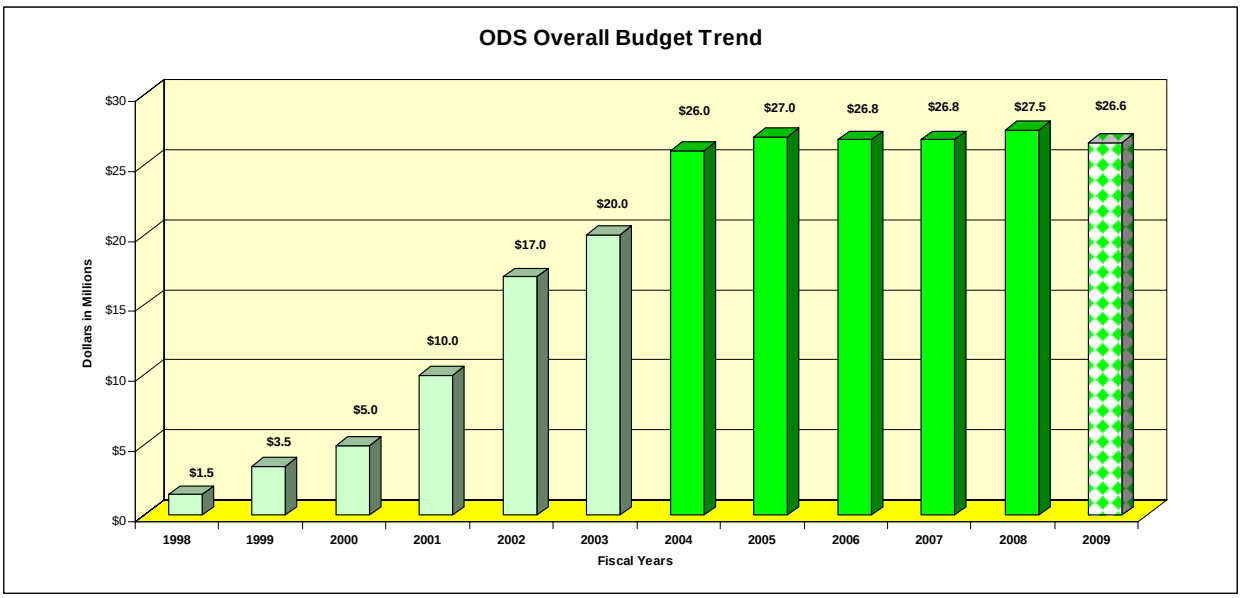
4. Promote and support the development and improvement of methodologies appropriate to the scientific study of dietary supplement ingredients.

5. Expand and conduct outreach efforts that inform and educate the public, health care providers, and scientists about the benefits and risks of dietary supplements.

ODS emphasizes research because of its responsibilities, as listed in the DSHEA, "to conduct and coordinate scientific research within the NIH relating to dietary supplements and the extent to which the use of dietary supplements can limit or reduce the risk of diseases." In Goal 5, the emphasis on outreach efforts is based on the ODS mission statement and the reference to education includes informing various stakeholders about dietary supplements and promoting research training.

ODS Budget

The ODS budget grew rapidly from 2000 to 2004; since 2004, the Office's budget has been relatively stable (darker green) (Figure 1). ODS's FY2008 budget was $27.5 million. The FY2009 President's budget request for ODS (stippled bar) is $26.6 million.



ODS Extramural Investments.

ODS's guidelines and criteria for initiating, expanding, or otherwise modifying its extramural investments have reflected DSHEA and congressional mandates. These guidelines are a response to gaps in scientific knowledge, requests for research support from investigators, requests for information, and available resources. ODS extramural investments are categorized into four broad areas: research support, research tools, communication, and science-policy interactions. The Office's key activities are grouped into 15 programs under these 4 areas (see below); these 15 programs capture most of ODS's activities.

The budget allocation for each of the four areas is included in the description of the areas. These budget figures are based on an FY2008 extramural budget of $22.3 million for grants, contracts, interagency agreements, and workshops. Another $5.2 million covers staff salaries and other expenses associated with ODS administration. Ninety-seven percent of the Office's extramural budget supports research grants and research tools. Communication and science-policy efforts rely heavily on investments of ODS staff time and expertise rather than direct funding.

An ODS staff member is responsible for overseeing each of the 15 ODS programs that supports extramural research, and most ODS staff members are active in more than one program. Each program interacts with one or more stakeholder communities, including research investigators; educators and teachers; health practitioners; research and educational institutions; agencies of the Federal government; dietary supplement, food, and related industries; media; consumer, and public interest groups; and members of the public. The 4 areas and 15 programs are described briefly below and in more detail in Part 3 of this report.

Area 1: Research support – 73% of ODS FY2008 extramural budget

1. Research grant portfolio. This portfolio consists of grants administered by NIH Institutes and Centers (ICs) that receive funding from ODS for research components related to dietary supplements. This investment supports the development of new knowledge on the health effects of dietary supplements.
2. Botanical Research Centers (BRCs). ODS established six centers in response to a congressional mandate. The Office administers the centers in partnership with the National Center for Complementary and Alternative Medicine (NCCAM). These centers expand the scientific base for botanicals used as dietary supplements.
3. Training and Career Development. These extramural investments primarily consist of cofunding for selected NIH research training and career grants. These grants enable junior scientists to develop a research program related to dietary supplements.
4. Conferences and Workshops. ODS funds research conferences and workshops primarily through NIH grant mechanisms, although it also supports conferences and workshops initiated by NIH. These conferences and workshops bring together key scientists to discuss and define the research needs for various dietary supplements.

Area 2: Research tools – 24% of ODS FY2008 extramural budget

5. Analytical Methods and Reference Materials (AMRM). ODS established this program in response to a congressional mandate and administers it primarily through contracts originated by ODS. Supporting the development of analytic methods and reference

materials for dietary supplements has been key to making informative studies of dietary supplements possible.

6. Surveys of Dietary Supplement Use. ODS provides intellectual and financial support to Federal agencies conducting national nutritional surveys that include use of dietary supplements.
7. Dietary Supplement Databases. ODS provides intellectual and financial support and leadership to Federal agencies that are establishing databases to enable the interpretation of survey data on public nutrition habits and use of dietary supplements. ODS and its Federal partners at the USDA, CDC, National Library of Medicine, and FDA have created a dataset of dietary supplement ingredients and are developing a comprehensive database of information on supplement labels.
8. Evidence-based Reviews. In response to encouragement from Congress, ODS provides intellectual and financial support, primarily to the AHRQ Evidence-based Practice Centers, to conduct reviews that are critical to determining the research needs for selected dietary supplements. These reviews are published on the AHRQ Web site and in peer-reviewed journals. Evidence-based reviews are key to identifying the status of scientifically validated knowledge about dietary supplements and the important gaps in research.

Area 3: Communications – Less than 2% of ODS FY2008 extramural budget. Communications are an integral part of ODS's ongoing outreach.

9. Communications. ODS's communication activities include a broad spectrum of outreach activities, such as the ODS Web site, exhibits, and public information pieces related to dietary supplements.
10. Computer Access to Research on Dietary Supplements (CARDS). ODS developed this consumer-friendly, Internet-based database in response to the DSHEA mandate to compile a database of scientific research on dietary supplements. CARDS contains information on federally funded research projects pertaining to dietary supplements.
11. International Bibliographic Information of Dietary Supplements (IBIDS). ODS developed this consumer-friendly, Internet-based database in response to the DSHEA mandate to collect and compile the results of scientific research related to dietary supplements. IBIDS provides access to bibliographic citations and abstracts from published, international, and scientific literature on dietary supplements.
12. Federal Dietary Supplement Working Group. ODS established the Federal Dietary Supplement Working Group in 2005 to share information and discuss issues related to dietary supplements among Federal agencies.

Area 4: Science-Policy Interactions – About 1% of ODS FY2008 extramural budget. These programs reflect the philosophy that good policy is founded on good science. ODS furnishes expertise in nutritional sciences to address public health issues related to dietary supplements.

13. Vitamin D Initiative. This initiative is an evolving partnership with NIH ICs and other Federal agencies through the Vitamin D Federal Working Group to address the research gaps related to vitamin D.
14. Dietary Supplement Use in the Military. This partnership with the DoD is evaluating the impact of dietary supplement use by military personnel.

15. Dietary Reference Intakes. ODS supports Federal programs to evaluate the reference standards for intakes of nutrients, including vitamins and minerals.

Evaluating ODS Investments

A comprehensive approach to the ongoing review and evaluation of ODS activities was an important component of the 2004–2009 strategic plan and ongoing evaluations continue to be a high priority for ODS. ODS held a public meeting in 2005 to engage stakeholders in evaluating its strategic plan. During this meeting, representatives of the ODS stakeholder community and other interested parties identified emerging needs and opportunities. A synopsis of the recommendations, presentations, and comments offered at this meeting are available at http://ods.od.nih.gov/Strategic_Planning_2004-2009/Public_Meeting_2005.aspx.

Another step in evaluating ODS activities involved analyses of needs and opportunities at ODS by external scientific panels and extramural contractors. These evaluations are described in the ODS program summaries.

To promote ongoing review and evaluation of ODS activities, ODS established the Federal Dietary Supplement Working Group and coordinated the group's first meeting in 2005. The working group enhances communications between ICs represented by the group and other Federal agencies interested in dietary supplement research. The working group meets twice yearly and serves as a forum for discussing dietary supplement-related programs, initiatives, and topics of common interest.

ODS Actions Addressing Strategic Goals: 2004–present.

As ODS develops its strategic plan for the next 5 years, it is reviewing the key activities established to achieve the five goals listed in its previous strategic plan. More detailed information on these activities is provided in the program summaries.

Goal 1. Expand the evaluation of the role of dietary supplements in disease prevention and reduction of risk factors associated with disease.

ODS cofunded grants for research on a broad range of topics related to disease prevention or reduction of risk factors for disease. Examples include:

- A clinical trial to evaluate the role of supplemental folic acid in reducing vascular complications following transplantation.
- A clinical trial to evaluate the role of supplemental vitamin D in reducing the progression of knee arthritis.
- An evaluation of whether supplementation with chromium picolinate can reduce insulin resistance in obese individuals at risk of type 2 diabetes.
- A study of the role of supplemental vitamin K in preventing fractures in children with cerebral palsy or other physical disabilities.
- A study of the mechanisms by which Saint John's wort affects the way that people respond to many prescription drugs

- A study of the efficacy of nighttime melatonin supplementation as a countermeasure to the side effects of beta-blockers.
- A clinical trial to evaluate the long-term effects of supplemental soy protein on the progression of atherosclerosis in postmenopausal women

ODS collaborated with other ICs in supporting funding opportunities for research on the roles of dietary supplements in ameliorating various disease states, such as the request for applications (RFA) for studies on "Mechanisms of Alcoholic and Nonalcoholic Fatty Liver."

ODS cofunded the training and career development of junior scientists with research interests relevant to dietary supplements. Some of these awards enabled selected NIH intramural scientists to expand their research into dietary supplements.

Goal 2. Foster research that evaluates the role of dietary supplements in maintaining and improving optimal physical and mental health and performance.

ODS staff have:

- Initiated the Vitamin D Federal Working Group to develop a vitamin D initiative that addresses research gaps related to the role of vitamin D in maintaining optimal health; an evidence-based review and ODS-cosponsored workshops identified these gaps.
- Collaborated with the U.S. Army Research Institute of Environmental Medicine in evaluating the use and safety of dietary supplements among soldiers.
- Partnered with National Health and Nutrition Examination Survey (NHANES) staff to evaluate the use of dietary supplements by Americans.
- Partnered with the CDC's National Health Interview Survey to study motivations for using dietary supplements.

In addition, ODS and its Federal partners have provided funds to the Institute of Medicine to evaluate the new Dietary Reference Intakes for key vitamins and minerals.

Examples of research cofunded by ODS include:

- The role of dietary supplements in promoting health, such as the role of specific dietary supplements in infant development and promoting a healthy pregnancy.
- The safety and efficacy of dietary supplements, such as a comparison of the efficacy of calcium phosphate to that of calcium carbonate in promoting bone health and a study of the role of calcium supplements in regulating body weight.
- Potential risks of dietary supplements in certain populations, such as an evaluation of the adverse effects of iron supplementation in HIV-infected pregnant women.
- The role of dietary supplements in maintaining health through a clinical trial in partnership with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to examine the role of saw palmetto (*Serenoa repens*) and pygeum (*Pygeum africanum*) in alleviating lower urinary tract symptoms in men with benign prostatic hyperplasia.

Goal 3. Stimulate and support research to further understanding of the biochemical and cellular effects of dietary supplements on biological systems and their physiological impact across the life cycle.

Studies on the mechanisms and impact of dietary supplements cofunded by ODS include:

- A study of how bitter melon juice improves the hepatic insulin signaling cascade and activates the mammalian longevity gene sirtuin (Sirt1) to prevent or treat diabetes.
- A study of whether selected gene-environment interactions are risk factors for obesity in the Yup'ik people by assessing the role of polyunsaturated fatty acids in regulating gene expression.
- A study of how trans-10, cis-12 conjugated linoleic acid reduces the triglyceride content of human adipocytes and the potential metabolic consequences of this activity, especially on the reduction of obesity.
- An NIH intramural project on the ability of polyphenols to improve metabolic and cardiovascular health.

Goal 4. Promote and support the development and improvement of methodologies appropriate to the scientific study of dietary supplement ingredients.

- ODS's AMRM program greatly expanded the development of approximately 18 validated analytical techniques and approximately 30 reference materials for identifying specific dietary supplement ingredients to meet the needs of investigators.
- The BRCs disseminated the results of new research on the chemical and biological characterization of botanicals as dietary supplements through a workshop at the 2007 Experimental Biology meeting as well as through peer reviewed publications.
- ODS has partnered with AHRQ and its Evidence-based Practice Centers to award contracts for evidence-based reviews of six key dietary supplements: omega-3 fatty acids, ephedra, vitamin D, soy, B vitamins and berries, and multivitamin/mineral (MVM) products.
- ODS has fostered the improved measurement of dietary supplement and nutrient intakes in population surveys through partnerships with the USDA and CDC's NHANES to support the development of ingredient and label-based databases for dietary supplements.

Goal 5. Expand and conduct outreach efforts that inform and educate the public, health care providers, and scientists about the benefits and risks of dietary supplements.

- ODS serves as a key information resource for DHHS and other Federal agencies through its comprehensive Web site and the Federal Dietary Supplement Working Group.
- ODS promotes the transfer and translation of information about dietary supplements in several ways, including providing extensive information on dietary supplements on the ODS Web site (ods.od.nih.gov) and in peer-reviewed journal articles, offering collaborative workshops on dietary supplements and publishing the reports on the ODS Web site, and supporting evidence-based reviews and publishing the results on the Office's Web site.

- ODS has enhanced access to ODS information and databases by improving its Web site design. ODS has enhanced and expanded the two databases mandated by the DSHEA, IBIDS and CARDS, for Web accessibility.
- ODS has expanded its communication activities by, for example, adding media resources to the ODS Web site, improving exhibition displays for national meetings, and posting resources on its Web site from the AMRM program. To "teach the teachers" about dietary supplements, ODS staff designed and offered an annual weeklong practicum on dietary supplements for academic, Federal, and industry researchers.

Fulfilling the Mission: Impact of ODS

A few examples of ODS activities related to specific dietary supplements, including the questions raised and the resolution of these questions, illustrate the impact of ODS activities on the health of the public. The vignettes in this section demonstrate how scientific information developed through research programs and with the use of research tools applied and coordinated by ODS in collaboration with Federal partners have impacted public health.

Ephedra

Ephedra-containing products were popular dietary supplements for promoting weight loss or enhancing athletic performance. By the late 1990s, evidence of adverse events and even deaths associated with these products began to accumulate. To assess the efficacy and safety of ephedra, ODS and NCCAM partnered with AHRQ to support an evidence-based review of ephedra by one of AHRQ's Evidence-based Practice Centers. The findings of this review were published in 2003 in the *Journal of the American Medical Association*. The review showed that ephedra promoted modest short-term weight loss but no data were available on its impact on long-term weight loss. Furthermore, the evidence was insufficient to support using ephedra to enhance athletic performance. Finally, the use of ephedra was associated with an increased risk of serious side effects, including heart palpitations and psychiatric, autonomic, and gastrointestinal symptoms.

The FDA cited this evidence-based review in 2004 when it determined that ephedra presented an unreasonable risk of illness or injury and prohibited the sale of dietary supplements containing ephedra.

By analyzing the available scientific information on ephedra, ODS and its partners helped to inform public policy. Moreover, because the FDA prohibited the sale of dietary supplements containing ephedra in the United States, ODS's activities have helped ensure that research funds that might have been spent on studying ephedra are available to fund research on other dietary supplements.

Chromium and Insulin Resistance

Chromium, a metal, is an essential nutrient but its mechanism of action is not known. Some studies have suggested that chromium as a dietary supplement could assist in the control of type 2 diabetes. ODS and its NIH partners supported an evidence-based review and a workshop in 1999 on the state of scientific knowledge about the role of chromium as an essential nutrient and whether chromium deficiency might play a role in certain disease states, particularly type 2 diabetes.

In 2001, ODS, NCCAM, and NIDDK sponsored a call for research applications on chromium as adjuvant therapy for type 2 diabetes and impaired glucose tolerance. ODS and its partners awarded eight grants that increased the amount of funding by NIH for this topic more than four-fold. The resulting research has advanced our knowledge about how chromium might act biochemically to enhance insulin action. Moreover, NIH-sponsored clinical trials are currently assessing whether chromium picolinate taken as a dietary supplement might help prevent or control type 2 diabetes.

Multivitamin/Mineral (MVM) Supplements

ODS's partnership with the NHANES study has enabled the collection of data on the use of dietary supplements by a nationally representative sample of the American public. Through this partnership, NHANES has documented the prevalence of MVM supplement use by Americans. Approximately one third of U.S. adults who participated in NHANES reported taking MVM supplements.

This finding led to the challenge of determining the benefits and risks associated with MVM use. ODS and the NIH Office of Medical Applications commissioned a review of MVM use and its impact on disease prevention by an Evidence-based Practice Center. The review concluded that few examples could be documented of disease prevention through MVM supplement use[3] and that the "current level of public assurance of the safety and quality of MVMs is inadequate."

This review formed the basis for the NIH State-of-the-Science Conference, Multivitamin/Mineral Supplements and Prevention of Chronic Disease, in 2006. The independent panel found that:

> *In general, MVMs are used by individuals who practice healthier lifestyles, thus making observational studies of the overall relationship between MVM use and general health outcomes difficult to interpret. Despite the widespread use of MVMs, we still have insufficient knowledge about the actual amount of total nutrients that Americans consume from diet and supplements. This is at least in part due to the fortification of foods with these nutrients, which adds to the effects of MVMs or single-vitamin or single-mineral supplements. Historically, fortification of foods has led to the remediation of vitamin and mineral deficits, but the cumulative effects of*

[3] Folic acid use by women of childbearing age to prevent neural tube defects in their offspring and the combination of calcium and vitamin D (but neither nutrient alone) have a beneficial effect on bone mineral density and fracture risk in postmenopausal women.

supplementation and fortification have also raised safety concerns about exceeding upper levels. Thus, there is a national need to improve the methods of obtaining accurate and current data on the public's total intake of these nutrients in foods and dietary supplements.

The conference proceedings are available at http://consensus.nih.gov/2006/2006MultivitaminMineralSOS028Statementhtml.htm.

ODS is actively working with Federal partners to address this national need on multiple fronts. Specifically, ODS is providing tools and resources for determining the upper safe limits for individual vitamin and mineral intakes; assembling a public database of dietary supplement label information; developing an analytically validated database of active ingredients in MVM supplements; improving analytical methods and reference materials for analyzing dietary supplements; refining survey questions to obtain better information on their use; and expanding its research on the basic biological mechanisms by which supplements might modify disease risks.

Vitamin D

Vitamin D is a unique nutrient because people can meet their vitamin D needs in two distinct ways: by endogenous production from sun exposure, and by eating foods and dietary supplements containing this nutrient. In addition to enhancing calcium metabolism, accumulating evidence indicates that vitamin D might play other roles in human health, including supporting immune function; reducing inflammation; and supporting cell proliferation, differentiation, and programmed cell death. Because vitamin D plays these important roles, vitamin D deficiency might contribute to various chronic diseases.

At a time when the importance of vitamin D to health has stimulated new research, concerns about the sufficiency of vitamin D levels in the U.S. population are growing. Reports of rickets (the classic vitamin D deficiency disease) and low blood levels of the biomarker of vitamin D status—25-hydroxyvitamin D—among various subgroups of the U.S. population raise questions about the effectiveness of current public health approaches to ensuring vitamin D adequacy.

ODS is uniquely situated within NIH to focus attention on these issues and to coordinate research on the many facets of vitamin D—research that includes several of the NIH ICs. These efforts began formally with the conference in 2003, Vitamin D and Health in the 21st Century: Bone and Beyond, co-sponsored by ODS and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). In 2007, AHRQ completed and released an evidence-based review, *Effectiveness and Safety of Vitamin D on Bone Health*, commissioned by ODS.

ODS, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Cancer Institute, and the American Society for Nutrition cosponsored a second conference, Vitamin D and Health in the 21st Century: An Update, in 2007 to address the issues raised in the review. The highlights of this conference were presented in a symposium at the 2008

Experimental Biology Annual Meeting in San Diego, California, on April 8, 2008, and published in a supplement to the *American Journal of Clinical Nutrition*.

One result of these efforts has been the formation of the Vitamin D Federal Working Group, which is translating the research needs in this area into actions by appropriate Federal research groups. The National Institute of Standards and Technology (NIST) is developing Standard Reference Materials (SRMs) for Vitamin D to facilitate analyses of vitamin D in foods and human fluids. The data on vitamin D collected through NHANES are being analyzed. The Food and Nutrition Board of the National Academy of Sciences is reconsidering the dietary recommendations for vitamin D. The NIH ICs are collaborating by providing funding opportunities to support research that will close the gaps in knowledge.

These efforts will take time to produce results but they are expected to offer valuable findings. Ultimately, ODS expects that its vitamin D-related activities will inform the reappraisal of the standards for Dietary Reference Intakes of vitamin D across an expanded set of conditions for maintaining human health.

Looking Ahead: The ODS Strategic Plan for 2010–2014

"…what's past is prologue…" (William Shakespeare, *The Tempest,* act II, scene i).

In addressing the future, ODS remains committed to its original mission of strengthening knowledge and understanding of dietary supplements through research, dissemination of research results, and public education.

This mission remains urgent. The number of products sold as dietary supplements has increased dramatically, from about 4,000 in 1994 to an estimated 50,000 in 2008, reflecting their wide use by the American public. Evaluating the exposure of the public to dietary supplement ingredients and the public health implications of this exposure is challenging. However, new insights into biologic processes are emerging, enabled by advances in the biomedical sciences and by the growing interdisciplinary approaches to scientific problems. The opportunities to strengthen knowledge and understanding of dietary supplements through research have never been greater.

The foundation for the 2010–2014 strategic plan will remain three-fold: the congressional mandates set forth by the DSHEA, the DSHEA definition of a dietary supplement, and the ODS mission statement. The programs established by ODS will be chosen for their potential impact on public health. ODS's priorities will reflect the input from Congress, ODS's Federal partners, the scientific community, industry, the public, and existing law. For each high-priority activity, ODS will identify its role and responsibilities, which might include providing leadership, collaboration, funding, staff support, or information. The plan will also include criteria for evaluating outcomes.

Based on internal discussions and input from ODS's Federal partners, ODS is considering the following strategies and actions for activities in 2010–2014 in its four focus areas. The current strategic goals will be modified as necessary to reflect the strategies and activities that are finally adopted.

Strategy for Research Support: **Maintain and strengthen the ODS commitment to supporting research as the fundamental component of developing new knowledge and applying that knowledge to public health issues associated with the use of dietary supplements.**

Potential activities:

- Continue to support NIH-sponsored research that is relevant to the ODS mission by cofunding grants.
- Continue to promote scientific study of the benefits of dietary supplements in maintaining health and in preventing chronic diseases and other health-related conditions.
- Continue to identify research partners and collaborative funding opportunities.
- Promote studies on the safety of dietary supplements and, especially, on biomarkers of toxicity and drug interactions.

- Encourage broader dissemination of information on research gaps and opportunities to partners who might have similar interests.
- Continue to develop research training mechanisms, such as the Dietary Supplement Research Practicum, to educate academicians, senior graduate students, and health care professionals.
- Encourage sabbaticals at and special assignments to ODS by outstanding academicians.
- Provide new doctoral level graduates with opportunities and skills to conduct dietary supplement research.

Strategy for Development of Research Tools: **Commit resources to the development and application of research tools as crucial aspects of supporting research.**

Potential activities:

- Accelerate analytical methods development and validation by identifying and prioritizing stakeholder needs and by funding development, optimization, and validation studies.
- Encourage the development, validation, and analysis of biomarkers of exposure, efficacy, and toxicity.
- Provide resources for the development and dissemination of tools that allow stakeholders to use analytical methods by expanding the NIST matrix SRMs program and by creating chemical calibration standards.
- Develop programs that allow laboratories to demonstrate analytical proficiency in analyzing dietary supplement ingredients.
- Encourage, through the BRCs, quality control for plant identification, processing, and chemical characterization; characterization of multiple active ingredients in botanicals and their synergistic effects; and identification of multiple targets of activity using contemporary technologies.
- In collaboration with other Federal partners:
    - Continue supporting the collection of dietary supplement label information by NHANES and other national surveys.
    - Continue developing an analytically validated dietary supplement database for key nutrients and other bioactive products of public health importance with the USDA's National Food and Nutrient Analysis Program.
    - Develop new methodologies for collecting information on dietary supplement use and reporting findings.

Strategy for Enhancing Communication: **Continue and expand efforts to communicate the results of scientific research broadly using appropriate means to reach different stakeholders.**

Potential activities:

- Redesign the ODS Web site to include a more consumer-friendly home page and enhance navigation and searching capabilities.

- Develop new electronic ODS fact sheets targeted to health professionals, consumers, and those with low literacy skills.
- Translate fact sheets and glossary into Spanish.
- Create a glossary of terms related to dietary supplements for consumers.
- Increase public access to the ODS e-mail list and create a consumer newsletter.
- Continue offering the Dietary Supplement Research Practicum and explore the development of electronic versions of this course.
- Expand the coverage of dietary supplement research in CARDS to include research by other Federal agencies, analyze trends in dietary supplement research funding, and increase recognition of CARDS as a reference source by investigators and administrators.
- Launch Clinical IBIDS, a version of IBIDS that disseminates information on publications reporting clinical studies of dietary supplements.
- Develop a consistent look for the Web site and ODS publications and exhibits.

Strategy for Science-Policy Interactions: **Based on the DSHEA mandates, ODS will continue to provide advice and counsel to colleagues in the Federal government on public health issues of mutual concern and responsibility.**

Potential activities:

- Identify emerging topics of public health significance that require or could benefit from evidence-based reviews.
    - Develop a state-of-the-science conference, consensus conference, or other conferences to discuss further the issues raised by evidence-based reviews.
    - As needed, develop trans-agency working groups on these topics.
- Explore the development of tools for improving the use of evidence-based reviews with high scientific quality, relevance to specific applications, and a broad range of possible applications in nutrition and dietary supplements.

The Future: Beyond 2014

Members of the public are increasingly taking personal responsibility for their own health. More and more people are using lifestyle interventions that include diets, dietary supplements, and physical activity to support their health and wellbeing and reduce the risk of chronic diseases. An urgent need exists to provide the public with accurate and reliable information about the impact of these interventions.

The ultimate goal of ODS-sponsored activities and programs is to provide current information about dietary supplements. ODS accomplishes this by continually evaluating current science, identifying gaps in the knowledge base, seeking relevant research strategies to fill those gaps, and translating the results of this research into useful information.

ODS proposes the following vision statement to describe the desired impact of ODS actions and programs:

> ***ODS Vision:*** *Consumers, health professionals, and government officials will have ready access to the latest and highest quality scientific information on the health effects of dietary supplements through the activities of the Office of Dietary Supplements.*

Examples of emerging needs and opportunities for dietary supplement research include:

- Analysis of nutrient intakes from dietary supplements. The tools and resources needed to advance the science of dietary supplements include questionnaires to determine the supplements that people are taking, a database of dietary supplement ingredients, a comprehensive label database, additional SRMs, and software to assess usual intakes. ODS is already developing these tools with its Federal partners.
- Biomarkers. A biomarker is a clinical entity—chemical or physical—that can be used to measure intakes, the progress of disease, or the effects of disease prevention or treatment. The challenge is to characterize biomarkers that can inform research on the biological effects of dietary supplements. More research on biomarkers of intake, disease progression, and outcomes is needed.
- Effective clinical study designs. The gold standard for clinical trial design is the randomized controlled trial in which patients are randomly assigned to a treatment or control group. However, randomized controlled trials are very expensive and difficult to carry out, particularly if the effect of the treatment is not large or takes a long time to develop, which is common in nutrition research. New clinical study designs need to be developed and validated to provide valuable information on nutrition-related interventions.
- Personalized nutrition. Science is at the threshold of making it possible to understand the complex interactions among diet, the environment, and genes that give rise to the diversity of human response. The focus in nutrition is shifting from dietary guidelines for populations to individualized diets. Research in this area will affect the ways in which people use dietary supplements in their personal health plans.
- New research visions. NIH has initiated the Human Microbiome Project with the mission of generating resources. This project will enable the comprehensive characterization of the microbial communities that are indigenous to humans and their roles in human health and disease. Dietary supplements contain potentially beneficial bacteria or yeast that can act as probiotics and influence the microbiome. NIH has also initiated an epigenetics initiative to nurture the study of factors that modify gene expression. ODS has collaborated with other ICs in supporting this effort. Epigenetics research may be key in exploring the basis of some effects of dietary supplements.

Your Input Influences the Future

In 2010–2014, ODS will complete its second decade. The Office seeks additional input on its 2010–2014 strategic plan not only from its Federal partners, but also from other stakeholders, including academic, government, and industry-based research communities; health care providers; educators; representatives of dietary supplement, food, and related industries; media outlets; consumer and public interest groups; and individuals and the public at large. ODS will develop its strategic goals for 2010–2014 after evaluating the input from all of its stakeholders.

WE WANT TO HEAR FROM YOU!

Ways to respond with comments and questions:

ODS E-mail: ODSPlan@od.nih.gov

ODS Web site: http://ods.od.nih.gov/strategicplan

ODS Webinars: ODS will hold a series of four webinars at the times and topics listed below to hear additional comments on and suggestions for ODS initiatives for possible inclusion in the 2010-2014 ODS Strategic Plan. The topic is taken from the four areas described in this background paper, *A Report to the Public*. Each webinar will begin with brief comments by a Federal partner and a stakeholder on the topic of that webinar. The remainder of each webinar will be devoted to hearing public comments. Participants should register in advance to make an oral comment of up to three minutes (see ODS Web site above

Research Support: Thursday, January 29, 2009, 1:00–2:00 pm EST
Research Tools: Tuesday, February 3, 2:00–3:00 pm EST
Science-Policy Interactions: Wednesday, February 11, 1:00–2:00 pm EST
Communications: Thursday, February 19, 2009, 2:00–3:00 pm EST

If you would like to participate in one or more of these webinars, register through the ODS Strategic Plan Web site: http://ods.od.nih.gov/strategicplan.

Note: All webinars will be archived on the ODS Strategic Plan Web site. So even if you cannot participate when the meetings take place, you can view the webinar and submit comments or questions at a later time.

Part 3: Program Activities

Section One: Research Support

In 1994, Congress approved the DSHEA, which ensured that consumers would have ready access to a variety of supplement products, including many containing botanical ingredients. The DSHEA also called for the establishment of the ODS at NIH with the mandate of stimulating and coordinating research on dietary supplements.

However, despite the widespread availability of supplement products and promising science on these products, biomedical research in this area was relatively limited. Four of the goals of the 1998-2003 and the 2004–2009 ODS strategic plans therefore addressed the need for more support of research on the role of dietary supplements in preventing disease and maintaining health, the biological effects of supplements, and methodologies for studying supplement ingredients:

1. Expand the evaluation of the role of dietary supplements in disease prevention and in reduction of risk factors associated with disease.

2. Foster research that evaluates the role of dietary supplements in maintaining and improving optimal physical and mental health and performance.

3. Stimulate and support research to further understanding of the biochemical and cellular effects of dietary supplements on biological systems and their physiological impact across the life cycle.

4. Promote and support the development and improvement of methodologies appropriate to the scientific study of dietary supplement ingredients.

Two ODS programs focus on the conduct of research:

- The **Research Grants Portfolio** consists of NIH research grants that ODS cofunds because of their relevance to advancing the science of dietary supplements. The Research Grants Portfolio accounts for the largest expenditure in the ODS budget.
- The **BRCs** are a joint effort with NCCAM and the Office of Research on Women's Health. These centers expand the scientific base for botanicals used as dietary supplements.

Two ODS programs focus on the development of research skills and experience:

- The **Training and Career Development** program supports training opportunities, largely for scientists early in their careers, to address research relevant to dietary supplements.
- The **Workshops and Conferences** program supports meetings that offer critical discussions on the state of the science in dietary supplements.

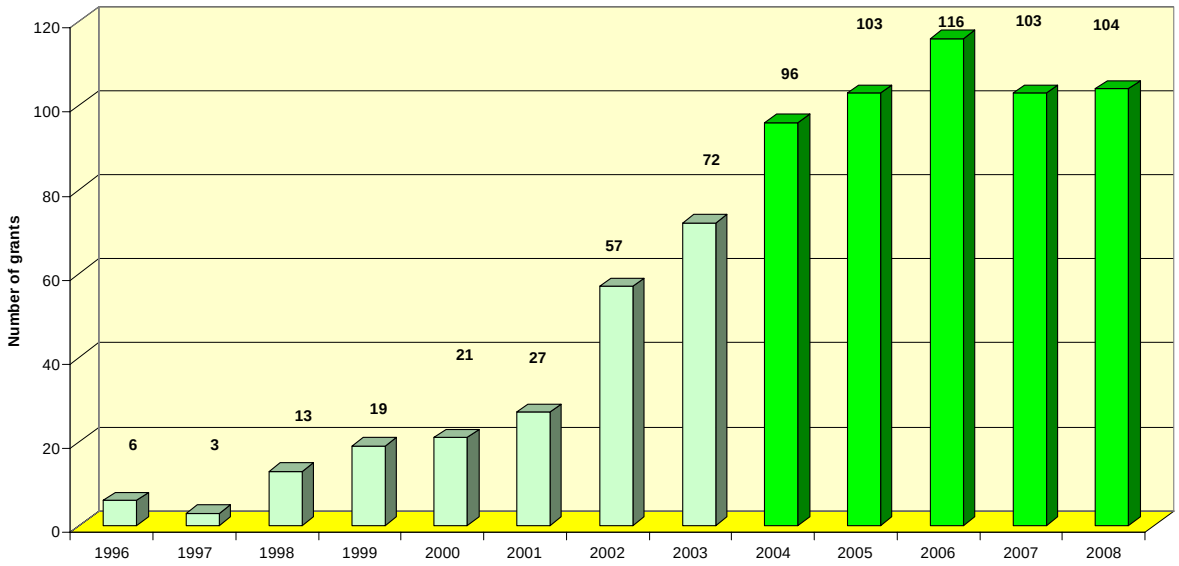
In FY 2008, these programs accounted for $16.2 million (73%) of the $22.3 million ODS spent on dietary supplement research. All of these programs support research primarily by funding NIH peer-reviewed applications. The four ODS research programs are described below.

I. Research Grants Portfolio

Scope of the Program. NIH supports research in our nation's laboratories and clinical facilities through grants selected on the basis of recommendations from peer-review panels. As an NIH Office, ODS does not have direct grant-making authority. ODS therefore works closely with the NIH ICs to cofund research that is relevant to dietary supplements.

Progress. The ODS portfolio of cofunded grants grew from 6 grants in 1996 to a peak of 116 in 2006 before dropping to 104 grants in 2008. Although the overall ODS budget grew rapidly in 1999–2004, it has been essentially flat since 2006, as has the overall NIH budget. The number of grants cofunded by ODS is presented in Figure 1. The total funding for FY2004–2008 is listed in the table below.

Figure 1: Number of ODS co-funded grants FY1998 - FY2008 (new and continuing)



FY 2004	96 grants	$14,527,341
FY 2005	103 grants	$17,377,312
FY 2006	115 grants	$16,841,439
FY 2007	103 grants	$16,020,769
FY 2008	104 grants	$15,483,094

Over the years, ODS has cofunded grants with 18 ICs using multiple funding mechanisms, such as investigator-initiated research, research training and career development, and conference grants. The ODS portfolio has included basic research (cell culture, in vitro, and in vivo) and clinical studies ranging from small pilot studies to large multicenter trials. Presently, ODS is listed as a cosponsor of 37 clinical studies on the NIH clinical trials Web site,

www.clinicaltrials.gov. ODS has representatives on the data safety and monitoring boards (DSMBs) of four ongoing clinical trials.

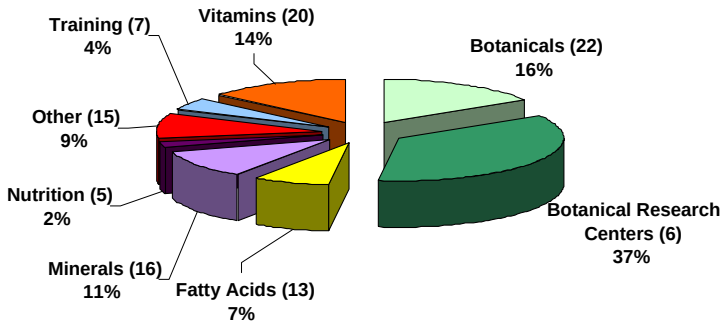
ODS has developed strategies to help identify grants of potential interest for cofunding. One strategy is to send a set of guidelines to NIH IC directors four times a year. These guidelines provide criteria for ODS cofunding and are accompanied by an invitation to ICs to seek cofunding from ODS for meritorious applications meeting the criteria.

ODS also works proactively to stimulate applications of interest by reviewing all of the funding opportunity announcements submitted by ICs to the NIH Office of Extramural Research through the Early Notification System. When ODS identifies a funding opportunity—either an RFAs or a program announcement (PA)—that has a component of interest to ODS, the office signs on as a potential cofunder and thereby informs the research community of the ODS interests. ODS has participated in more than 150 such funding opportunities and contributed to the budgets of approximately 80 grants resulting from these cosponsored announcements.

By developing cofunding strategies, ODS has leveraged its funds to support dietary supplement research by NIH. For every dollar that ODS invested in research related to dietary supplements in 2007, the NIH ICs invested 17 dollars.

The topics addressed by the studies in the ODS grants portfolio are diverse, ranging from classical nutrients to emerging botanicals and other natural products. Figure 2 provides a breakdown of the 104 grants cofunded by ODS in FY 2008 by topic; the graph also includes data on the numbers and percentages of training and BRC grants.

Figure 2: ODS Funding FY 2008: Percent $ by Topic
(Number of grants in parentheses)



ODS has developed an internal database, the Grant Efficiency Management System (GEMS), to track the grants that receive ODS funding. GEMS allows ODS to monitor the scope and dimensions of its grant funding.

In 2006, ODS began providing 1-year limited funding for intramural research projects on a competitive basis. One aim of this activity has been to support the work of postdoctoral fellows and non-tenured scientists and help them establish independent research careers. This program has also provided ODS with an additional opportunity to educate the NIH intramural community about the ODS mission and goals.

Lessons Learned. Continuous outreach to the NIH ICs and the research community to encourage research on dietary supplements has been essential. ODS has learned to be proactive in seeking out funding initiatives. ODS has identified opportunities for potential cofunding by monitoring and responding to the Early Notification System through which NIH ICs announce the solicitation of proposals on special research topics,

Plans for the Future. ODS has established or participated in multiple working groups with NIH ICs to help identify promising opportunities for supporting research that is relevant to the ODS mission. ODS will continue and expand its participation in relevant working groups.

Additional Information on the Research Support Program

- A complete list of grants cofunded by ODS by fiscal year is available on the ODS Web site, at http://ods.od.nih.gov/Funding/Grants__Contracts.aspx.
- A copy of the memo sent to the NIH Institute and Center Directors seeking grants to cofund is in Appendix B.

II. Botanical Research Centers

Scope of the Program. ODS started the BRC program started in 1999 with congressional funding to "expand [ODS's] efforts and develop a botanical research center initiative with major research institutions across the nation." The goal of the BRCs is to identify potential health benefits of dietary supplement botanicals and address concerns about their safety.

ODS, in collaboration with NCCAM and the Office of Research on Women's Health, currently funds six Dietary Supplement Research Centers focused on botanicals as part of the NIH BRC program. These centers support botanical research ranging from plant identification to early-phase clinical studies, but their emphasis is on preclinical research.

Progress. In 2003, the three major NIH cosponsors of the original BRCs (ODS, NCCAM, and the National Institute for Environmental Health Sciences) convened an expert panel to assess the BRC program. The panel recommended that NIH continue the BRC program but that all of the centers provide:

- High-impact research theme
- Studies of basic mechanisms and human health, with a high level of translational interaction between the two
- Innovative technology
- Emphasis on quality assurance and quality control

The expert panel stated that the overall program should emphasize preclinical research to inform potential clinical studies of botanical dietary supplements, with preliminary clinical research as an option rather than a requirement. The panel also concluded that an emphasis on product quality and innovative technology would best serve the field. Based on these recommendations, NCCAM and ODS solicited applications in 2004 and 2006 and subsequently funded six centers, including three of the original centers. NIH plans to announce a recompetition for new and continuing centers in 2009.

The BRCs have built multidisciplinary research teams. They also use contemporary technologies and emphasize the complexity of human biology. The six centers offer a range of expertise areas, including early-phase clinical studies, natural products research focused on botanicals, and the use of contemporary methodologies. The centers also provide an outstanding training environment for future leaders in research that is relevant to dietary supplements. Finally, the centers offer many networking opportunities for researchers interested in dietary supplements research; for example, the center directors hold annual meetings to share progress and these meetings can foster new collaborations.

Each center has a different research theme and focuses on studies with high potential for translation into benefits for human health. For example, one center is studying the actions of botanical oils that are rich in omega-3 fatty acids and the potential of these fatty acids to prevent inflammatory diseases, such as atherosclerosis. Another center is examining the ways in which selected botanicals influence the molecular, cellular, and physiological mechanisms of insulin resistance. Other centers are conducting research on botanicals that might play a role in preventing inflammation, alleviating the symptoms of menopause, or promoting antiviral activity.

Very early in the evolution of the BRC program, BRC investigators recognized that the complexity of botanical materials presented unique challenges. In contrast with synthetic drugs, botanicals (even as extracts) are complex mixtures of bioactive constituents that may have synergistic or antagonistic effects. These and other challenges could only be addressed by applying or modifying contemporary research tools. For example, some investigators have used such technologies as high-throughput bioassay-guided fractionation to identify potential bioactive constituents and are using current proteomics and mass spectrometry methodology to identify functional proteins in target tissues. Mass spectrometry has also been very useful in assessing the bioavailability, distribution, metabolism, and excretion of radiolabeled phytochemicals. The centers have shared their research methodologies and made them available to the broader research community through publications and presentations at meetings. In 2007, the BRCs organized a workshop featuring their current research at Experimental Biology 2007 and their presentations were summarized in a supplement to the *American Journal of Clinical Nutrition* (2008;87[2]:471S-513S).

The BRCs have developed quality-control procedures unique to botanical test materials. For example, BRC researchers have authenticated starting materials and prepared voucher specimens. Centers have also characterized chemicals and assessed the stability of botanical test materials.

Lessons Learned. It has taken time to develop a centers program in the relatively new area of botanicals research. Effective leadership within each center has been essential. The success of the program has also depended on the ability of several groups of investigators to participate actively in collaborative research.

Plans for the Future. ODS plans to encourage center scientists to continue developing new methods for botanicals research and sharing these techniques with the research community. ODS will also explore the feasibility of bringing the centers together as a network to better facilitate collaborative research.

Additional Information on the BRCs

- Information on the six institutions funded by BRC Program in 2005–2009 is on the ODS Web site, at http://ods.od.nih.gov/Research/Dietary_Supplement_Research_Centers.aspx. The site provides links to the Web sites for each center; these sites provide more detailed information on center activities.
- NCCAM maintains a Web site featuring the BRC Program at http://nccam.nih.gov/training/centers/#b.
- The papers from the workshop at Experimental Biology 2007 that were published as a supplement to the *American Journal of Clinical Nutrition* are listed in Appendix C.

III. Training and Career Development

Scope of the Program. ODS supports opportunities for individuals interested in pursuing a career in research on dietary supplements and related areas. The goal of the ODS support for training programs is to ensure that a sufficiently large, diverse, and highly trained workforce with appropriate knowledge and skills is available to assume leadership roles in addressing emerging research issues that are relevant to dietary supplements. ODS partners with NIH and other Federal agencies that share this goal to identify investigators to support.

Progress. ODS supports several training opportunities for those interested in research on dietary supplements. Since 2004, ODS has initiated a practicum in dietary supplements and an NIH seminar series; the Office has also expanded its travel award program.

Current ODS training activities are described below.

Extramural Activities - ODS has cofunded, with several NIH ICs, a variety of training and career development opportunities in dietary supplements and nutrition research. Current partners include NICHD, the Office of Research on Women's Health, the National Institute of General Medical Sciences, and the Fogarty International Center.

Intramural Activities - ODS has provided funding for the training and career development of non-tenured scientists in NIH intramural programs who are conducting research on dietary supplements.

Transagency Activities - ODS has provided funding for training and career development awards at other government agencies that are engaged in collaborative activities to further the ODS mission. These awards include postdoctoral fellowships at NIST for research on reference material development and at the USDA's Agricultural Research Service for methods development research on bioactive components of foods and dietary supplements.

Practicum – ODS commissioned the 2006-2007 Survey of Academic Nutrition, Food Science, and Allied Health Departments to evaluate the availability of training opportunities related to dietary supplements. When the survey revealed that training was not available, ODS created the Dietary Supplement Research Practicum to "train the trainers." The 5-day practicum, offered in 2007 and 2008 on the NIH campus, brings together faculty members, doctoral students, and postdoctoral fellows at academic institutions; health care providers; and other professionals with a biomedical degree. The practicum provides a thorough overview of issues, concepts, controversies, and knowledge gaps related to dietary supplements research.

Travel Awards - ODS has sponsored Young Investigator Travel Awards for predoctoral candidates and postdoctoral fellows conducting nutrition and dietary supplement research. These awards enable young investigators to participate in conferences and the ODS research practicum. ODS provides approximately 25 to 50 travel awards to trainees each year.

NIH Seminar Series – ODS organizes a seminar series at NIH in which noted researchers in the dietary supplements field present lectures on their current work. These lectures are open to scientists in the greater Washington, DC, metropolitan area.

International Training – The Fogarty International Center of NIH supports the Global Research Initiative Program for New Foreign Investigators (GRIP). GRIP promotes productive re-entry of NIH-trained foreign investigators into their home countries. GRIP is part of a broader program to enhance the scientific research infrastructure in developing countries; stimulate research on a wide variety of-high priority, health-related issues in these countries; and advance NIH efforts to address health issues of global import. ODS has provided funds for this program.

Lessons Learned. ODS has learned that the best method of providing opportunities for individuals interested in pursuing a research career in dietary supplements is to network with NIH ICs and other Federal agencies that share ODS's scientific goals. These partners have competitive training programs to support the best candidates and can bring appropriate candidates to ODS for cofunding.

Plans for the Future. ODS will evaluate its Dietary Supplement Research Practicum. If the practicum remains popular and timely, ODS might shift responsibility for conducting the program from its own staff to a contractor. This change would allow ODS to offer the course more frequently or to more diverse professional groups.

ODS plans to accommodate a visiting professor for a sabbatical and special assignments at ODS. ODS also plans to bring a recent doctoral program graduate to ODS to develop skills in dietary supplement research. These programs will provide ODS with the input and assistance of professional personnel.

Additional Information on the Training and Career Grants program

- Information on the 2008 ODS Dietary Supplements Research Practicum is available on the ODS Web site, at http://odspracticum.od.nih.gov/.
- The training and career grants supported by ODS in FY2007 are listed in Appendix D.
- A list of seminars offered by ODS in FY2007 is in Appendix D.

IV. Conferences and Workshops

Scope of the Program. ODS plans, organizes, and supports conferences, workshops, and symposia on scientific topics related to dietary supplements. These programs are designed to identify research opportunities and needs and to stimulate investigation. Although ODS can initiate conferences and workshops on its own, the office implements most of these programs in collaboration with NIH ICs, other government agencies, and professional and scientific organizations. Since its inception, ODS has cosponsored more than 150 scientific meetings focused on research promotion and dissemination. ODS welcomes proposals to cofund conferences and workshops on a quarterly basis through IC cofunding announcements.

Progress. ODS cosponsored more than 90 scientific meetings in 2004–2007. In many cases, ODS's primary role was to provide financial support for the portions of these meetings that covered topics of relevance to the ODS mission. The topics of these conferences and workshops have been diverse and far-reaching, including basic and applied research issues of interest to both ODS and other funding ICs and agencies. Several workshops and conferences cosponsored by ODS have led to the development of funding opportunities for topics of mutual interest to various ICs and ODS.

Some scientific meetings cosponsored by ODS have addressed research needs and opportunities related to specific populations. For example, beginning in 2004, ODS has cosponsored a series of conferences examining dietary intakes and blood levels of vitamin D, as well as vitamin D's role in maintaining health and/or contributing to disease at different stages in the lifespan. The identification of research gaps identified in these workshops provided the impetus for the vitamin D initiative described in Section Four.

In addition, ODS cosponsored the State-of-the-Science Conference on Multivitamin/Mineral Supplements and Chronic Disease Prevention in 2006. Conference participants raised the need for databases with information on the composition of MVM supplements. ODS is addressing this need by developing label and composition databases and supporting analytic methods for assaying these components, as described in Section Two.

Furthermore, ODS has been invited to develop scientific sessions for a number of academic and industry audiences. For these sessions, ODS has assisted in agenda development and selection of speakers. ODS often posts PowerPoint slides from these presentations on its Web site for wider distribution.

A unique opportunity for ODS has been its participation in meetings of the Consortium for the Globalization of Chinese Medicine. Much of this effort has focused on issues related to product characterization and quality. This program therefore has particular relevance to the ODS AMRM program (described in Section Two).

Lessons Learned. Initiating and cofunding conferences and workshops has been useful for stimulating not only awareness of the need for research on dietary supplements among investigators, but also for developing research support programs with both public and private sector funders.

Active sponsorships of workshops and conferences demand considerable ODS staff time. ODS must consider these demands when evaluating which conferences and workshops the office can actively sponsor.

Plans for the Future. ODS will work with its partners to develop a mechanism for identifying emerging workshop topics. ODS will also encourage greater dissemination of, and efforts to address, the research gaps and opportunities identified in the workshops and conferences it cosponsors.

Additional Information on the Conferences and Workshops program

- A list and description of conferences and workshops in which ODS played a major role is available at http://ods.od.nih.gov/News/Conferences_and_Workshops.aspx.
- Conference grants (R13 awards) cosponsored by ODS are on the ODS grants page, at http://ods.od.nih.gov/Funding/Grants__Contracts.aspx.
- A list of recent publications from ODS conferences and workshops is in Appendix E.

Section Two: Development of Research Tools

The development and improvement of methodologies for the scientific study of dietary supplement ingredients are key not only to advancing the science, but also to providing accurate information about dietary supplements to the public. According to an NHANES report published in 2004,[4,5] more than 50% of American adults report using a dietary supplement within the past month. The widespread use of dietary supplements underscores the importance of monitoring the composition of these products.

Goal 4 of the 2004-2009 ODS strategic plan was to promote and support the development and improvement of methodologies appropriate to the scientific study of dietary supplement ingredients**.** Four ODS programs address this goal:

- The **AMRM** program has expanded ODS's efforts to promote the development of the analytic methodologies and reference materials needed to study dietary supplements properly.
- The **Ingredient and Label-based Databases** program supports the development of label and ingredient databases as critical tools for nutritional research.
- The **Surveys of Dietary Supplement Use** program helps develop survey questions and gives financial support to surveys that collect information on the use of dietary supplements by the American people.
- The **Evidence-based Review** program supports evidence-based reviews on popular dietary supplements to identify what is known about the health effects of these supplements and gaps in research.

All of these resources provide tools for dietary supplement research to both the industrial and academic research communities.

In FY2008, ODS awarded $5.4 million (24%) of the $22.3 million it spent on research to research tools development. ODS made most of these awards through interagency agreements to other Federal agencies, such as AHRQ and USDA, to support the programs described in this section.

I. Analytical Methods and Reference Materials

Scope of the Program. ODS created the AMRM program in 2002 in response to congressional direction. The AMRM program goals are to build an infrastructure and provide funding to support the development of validated methods and reference materials for assessing product quality and to make these methods and reference materials readily available to the user community.

[4] Millen AE, Dodd KW, Subar AF. Use of vitamin, mineral, non-vitamin and non-mineral supplements in the United States: the 1987, 1992 and 2000 National Health Interview Survey results. J Am Diet Assoc. 2004;104: 942-50.
[5] Radimer KL, Bindewald B, Hughes J, Ervin B, Swanson C, Picciano MF. Dietary supplement use by US adults: Data from the National Health and Nutrition Examination Survey (NHANES) 1999-2000. Am J Epidemiol. 2004;160:339-49.

Progress. In the past 5 years, analytical chemists, dietary supplement researchers, and others concerned about dietary supplement analytical methodology have formed a research community. In the 2 years before the launch of the ODS AMRM program, the *Journal of AOAC International*—which publishes articles about research on validated methods for analyzing, among others, foods and food supplements—had no dietary supplement publications. Between the launch of the program in 2002 and January 2007, the journal published more than 100 articles on dietary supplement methods.

The AMRM program has made possible significant methodological advances in dietary supplements research since 2003. The program has accomplished this by identifying Federal and private laboratories with expertise in developing analytic methods and reference materials and funding projects in these laboratories through interagency agreements or contracts.

Methods Validation. The ODS cofunded, with the FDA's Center for Food Safety and Applied Nutrition, a contract with AOAC INTERNATIONAL to create 15 AOAC® Official Methods of Analysis℠ (http://www.aoac.org/vmeth/oma_program.htm) for dietary supplements. A collaboration of AOAC representatives and other stakeholders identified the supplement ingredients on which more research is needed and established priorities for the order of study. Eighteen methods have been validated by at least 8 laboratories and 10 have been approved as Official Methods of Analysis. Collaborative study reports have been published on nine of these methods, and articles on the other nine are in press.

Methods Development. ODS provided funding to the USDA's Food Composition and Methods Development Laboratory (http://www.ars.usda.gov/main/site_main.htm?modecode=12351500) to develop and optimize analytical methodology for extracting and measuring flavonoid glycosides. The funding also supported the development of chemical fingerprinting and chemometric techniques to verify the identity of botanicals.

ODS provided funding to the FDA's Center for Food Safety and Applied Nutrition (http://www.cfsan.fda.gov/list.html) to develop, optimize, and validate analytical methods for toxic elements, pesticides, and certain mycotoxins that have been reported to be contaminants in some dietary supplements.

Investigators have published the results of an ODS-sponsored study to validate thin-layer chromatographic fingerprinting methods for determining the botanical identity of 15 herbs in commerce.

Reference Materials. ODS provided funding to NIST to produce 20 suites of NIST Standard Reference Materials (SRM™) (http://www.cstl.nist.gov/programs/food.htm). A suite consists of supplement raw materials and finished products. Certified values for selected chemical constituents of these materials and products are established using a rigorous standard approach. Analysts use the SRM to verify whether their analytic instrument is operating properly and whether the assay has been performed correctly. Five suites of NIST SRM are now available and more are in development.

ODS has supported the research, development, production, and dissemination of calibration standards and analytical reference standards through the U.S. Pharmacopeia (http://www.usp.org/referenceStandards/) and other organizations. To date, the program has established contracts to produce nine U.S. Pharmacopeia reference materials and approximately 20 other materials for use in collaborative and precollaborative studies.

ODS has supported a pilot project to produce an electronic version of a handbook of botanical microscopy to replace the hard-copy version developed 100 years ago.

Education. ODS has funded the development and offering of short training courses for stakeholders in botanical microscopy, single-laboratory validation of analytical methods for dietary supplements, and design and conduct of collaborative studies.

Lessons Learned. An expert panel reviewed the AMRM program in 2006. The panel agreed that the program has successfully increased awareness of the need for good analytical methodologies and reference materials to promote quality control and standardization. The panel's major recommendation was to increase the pace of methods validation and reference material development.

At a stakeholders meeting in September 2007, participants encouraged the program to put more emphasis on the single-laboratory validation process for analytical dietary supplement methods because this is the foundation for developing official methods of analysis. The stakeholders also encouraged the AMRM program to work with the BRCs to promote process validation for the analyses of botanicals. Finally, the stakeholders recommended that ODS add more information to its Web site on the status of the activities supported by the AMRM program.

ODS sponsored a public meeting, the Vitamin Methodology Workshop, in July 2008 to evaluate the state of analytical methodology for vitamins in dietary supplement products and identify gaps in methodology. Twenty expert speakers made presentations and 30 representatives from research institutions, industry, regulatory agencies, and other ODS stakeholders contributed to the discussions. Participants composed an initial list of priorities for vitamin methods based on the public health impact and current state of the science; they also identified potentially promising approaches to analysis. An executive summary of the workshop will be posted on the ODS Web site.

Plans for the Future. The AMRM program will seek ways to speed up the development of analytical methods and reference materials for dietary supplements. In particular, ODS will seek to increase its support for developing single-laboratory validation processes for analytical methods, as suggested by the stakeholder meeting and the expert panel review. The program will give priority to laboratory methods for vitamins and minerals because they account for about 75-80% of the dietary supplements used in the United States.

Additional Information on the Analytical Methods and Reference Materials program

- A list of current and pending materials and methods as well as recent publications from ODS staff on the AMRM program is in Appendix F. ODS is updating the AMRM Web page on the ODS Web site to add detailed information on the validated methods and reference materials that the program has developed. This information will be available at http://dietary-supplements.info.nih.gov/Research/Analytical_Methods_and_Reference_Materials_Program.aspx .
- The Web site for the AOAC INTERNATIONAL Official Methods of Analysis℠ for dietary supplements is at http://www.aoac.org/vmeth/oma_program.htm.
- The Web site for the USDA's Food Composition and Methods Development Laboratory is at http://www.ars.usda.gov/main/site_main.htm?modecode=12351500.
- The Web site for the FDA Center for Food Safety and Applied Nutrition is at http://www.cfsan.fda.gov/list.html.
- The Web site for the food and nutritional products from the NIST Chemical Science and Technology Laboratory is at http://www.cstl.nist.gov/programs/food.htm.
- The Web site for the U.S. Pharmacopeia Reference Standards is at http://www.usp.org/referenceStandards/.

II. Surveys of Dietary Supplement Use

Scope of the Program. Surveys on the use of dietary supplements are critical for collecting information on the role of dietary supplement use in maintaining health. Since 1999, ODS has supported the collection of data on dietary supplement use as part of the ongoing NHANES. ODS has also partnered with other agencies in collecting data on the public's use of dietary supplements. In addition, ODS staff actively analyze and report the results of survey data on dietary supplements.

Progress. In 2004, NHANES and ODS staff published results from NHANES data on dietary supplement use in adults.[6] In 2007, NHANES and ODS staff published information on dietary supplement use in children and adolescents based on NHANES data.[7] ODS has increasingly worked with the NHANES program to measure data on nutrients that are found in foods and dietary supplements, such as folic acid, vitamin B12, and vitamin D.

In 2005, ODS began collaborating with NCCAM to fund a special supplement to the National Health Interview Survey (NHIS) on motivations for dietary supplement use. These data will provide additional information on the use of dietary supplements.

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[6] Radimer K, Bindewald B, Hughes J, Ervin B, Swanson C, Picciano MF. Dietary supplement use by US adults: data from the National Health and Nutrition Examination Survey, 1999-2000. Am J Epidemiol. 2004 Aug 15;160(4):339-49.

[7] Picciano MF, Dwyer JT, Radmier KL, Wilson DH, Fisher KD, Thomas PR, et al. Dietary supplement use among infants, children, and adolescents in the United States, 1999-2002. Arch Pediatr Adolesc Med. 2007 Oct.;161(10):978-85.

In 2004 and 2005, ODS conducted a series of secondary analyses of national survey data from proprietary sources under a contract with the Natural Marketing Institute. The analyses supplemented existing information on patterns of and motivations for use of less commonly consumed dietary supplements. ODS and NCCAM staff submitted questions based on the data for the NHIS and ODS staff have used these data for several presentations. This collaboration led to a partnership between ODS and the Natural Marketing Institute to analyze supplement use in military personnel and related behavior patterns.

Lessons Learned. ODS has assisted in expanding the NHANES to include information on dietary supplements. This expansion has provided valuable information on the use of dietary supplements. In addition, partnerships with other Federal agencies have been fruitful for collecting information on the use of dietary supplements by the American public.

Plans for the Future. ODS will continue to work with the NHANES program to ensure that the survey collects data on intakes of dietary supplements and clinical measures of interest. The office will also continue its efforts to ensure the inclusion of questions related to dietary supplements in other national Federal surveys.

Additional Information on the Dietary Surveys Program

- Recent publications by ODS staff in the Dietary Surveys Program are listed in Appendix G.

III. Ingredient and Label-based Databases for Dietary Supplements

Scope of the Program. The program's goal is to document the composition of dietary supplements in dietary supplement databases. This information is necessary to estimate accurately how much of a given ingredient is actually ingested by participants in surveys of dietary supplements and, ultimately, to determine whether nutrient intakes are excessive or deficient. The program compares values provided by the manufacturer with values from independent testing and these values will be available to the public through an online database. Such data can be used to enhance the quality, efficacy, safety, and public health impact of dietary supplements.

ODS has contributed financially and intellectually to the development of two Federal dietary supplement databases:

- National NHANES Dietary Supplement Label Database
- Dietary Supplement Ingredient Database (DSID)

NHANES collects data from a nationally representative sample of approximately 5,000 non-institutionalized civilians in the United States each year. The NHANES group at the National Center for Health Statistics developed the NHANES Dietary Supplement Label Database in 1999 to document intakes of the dietary supplements reported in its survey. ODS has played an active role in enhancing this database, which contains label information on the dietary supplements that NHANES respondents report using to determine the amount ingested of each ingredient. This database houses information provided by dietary supplement manufacturers.

ODS and the USDA's Agricultural Research Service began developing the DSID in 2003. The database contains independently determined analytic values for dietary supplement products, such as MVM products. The database builds on the food composition databases developed by USDA.

Progress. National NHANES Dietary Supplement Label Survey Database. ODS and the NHANES staff began developing the NHANES Dietary Supplement Label Survey Database in 1999 and released it to the public in 2003. ODS and the NHANES group have issued regular updates to the database since 2003. However, stakeholders have reported that the public release format is incomplete and difficult to use.

A congressional request led ODS to explore the feasibility of developing a new Internet-accessible database of proprietary label information and associated dietary supplement ingredients. ODS and the National Library of Medicine are using the Dietary Supplement Labels Database developed by the National Library of Medicine as the portal for the new online database. ODS has awarded a contract for improving and expanding the National Library of Medicine database and the project is currently in its pilot phase.

DSID. The USDA's Nutrient Data Laboratory and Food Composition Laboratory have been major collaborators in developing the DSID. A working group with representatives from several agencies has met monthly to establish priorities for the analytical work to enhance the database and to steer the database development in the appropriate direction. The working group identified 23 critical dietary supplement ingredients of public health interest based on such factors as extent of exposure, frequency of consumption, availability of analytical methods and reference materials, and Federal agency interest. For example, ODS has promoted the development of critical dietary supplement ingredients for which reference materials and analytical methods are lacking through the AMRM program.

The working group organized a 2004 pilot study to develop analytic methods for dietary supplements, including sample-handling procedures, for seven of the high-priority vitamin and mineral nutrients in dietary supplements. Based on the results of the pilot study, ODS commissioned a study in 2005 on 35 MVM supplement products marketed to adults to measure nutrient content and assess product variability. The study found that the mean levels of nutrients in 7 of 19 products were significantly different (by 14-46%) from the values claimed on the labels. These results underscore the need for independent testing of nutrient levels for the database.

Lessons Learned. National NHANES Dietary Supplement Label Database. The involvement of the DSID working group in monthly Dietary Supplement Label Survey Database meetings has facilitated progress in developing this database. The development of databases for all dietary supplement labels will, if successful, increase the currency and availability of information on dietary supplement use.

DSID. ODS has formed a partnership with several Federal agencies to document the need and advance the development of the DSID. The working group's recommendations have enabled ODS to prioritize the needs for analytical methods and reference materials.

Plans for the Future. ODS will continue to support the development of label databases, including the NHANES Survey Label Database and the ODS/National Library of Medicine dietary supplement label database. ODS will also continue to support the development of the DSID. ODS might need to support ongoing studies of the differences between declared label and actual analytical values.

In the long term, ODS will promote the merger of ingredient and label databases into one user-friendly, online database containing information on the ingredients of all dietary supplements sold in the United States. This database should incorporate the labels databases under development with the National Library of Medicine, the analytically validated database being developed with the USDA, monographs on key ingredients, and links to key references. These data will complement food composition data. The data will also be critical for assessing the total intake of nutrients and other components from foods and supplements to determine their impact on public health.

Additional Information on the Ingredient and Label-based Databases for Dietary Supplements Program

- A list of current dietary supplement databases is in the health information section of the ODS Web site, at http://ods.od.nih.gov/Health_Information/Health_Information.aspx.

- Recent publications by ODS Ingredient and Label-based Databases for Dietary Supplements Program staff are listed in Appendix H.

IV. Evidence-Based Reviews

Scope of the Program. In FY 2001, Congress instructed ODS to review the current scientific evidence and identify research needs related to the efficacy and safety of dietary supplements. ODS responded by developing an evidence-based review program for selected dietary supplements in partnership with AHRQ's Evidence-based Practice Centers Program. ODS also supports evidence-based reviews in partnership with the NIH Office of Medical Applications of Research, which sponsors NIH state-of-the-science and consensus development conferences.

Progress. ODS has supported evidence-based reviews by AHRQ on the safety and efficacy of the following dietary supplements and products:

- B vitamins and berries
- Ephedra
- Multivitamin/mineral products
- Omega-3 fatty acids
- Soy
- Vitamin D

ODS cosponsored a series of reviews with other NIH ICs on omega-3 fatty acids, including the role of omega-3 fatty acids in asthma, cancer, cardiovascular disease, child and maternal health, cognitive function, eye health, glycemic control, mental health, and organ transplantation. AHRQ has posted the results of these reviews on its evidence-based practice Web site.

ODS and the NIH Office of Medical Applications of Research cosponsored a review of MVM supplements for the NIH State-of-the-Science Conference on Multivitamin/Mineral Supplements and Chronic Disease Prevention in 2006. A major conclusion of the conference was that although MVM supplements are generally assumed to be safe, limited available evidence supports this assumption. One recommendation relevant to ODS was to develop new MVM supplement databases that describe the composition of supplements, update the databases on a continuous basis; and make the databases available to the research community.[8]

ODS cosponsored the 2007 publication of an evidence-based review[9] on vitamin D and a related conference, Vitamin D and Health in the 21st Century. ODS is currently leading an initiative with NIH ICs to develop a research agenda for vitamin D.

Lessons Learned. ODS has identified the following lessons from its experience in developing evidence-based reviews in collaboration with AHRQ:

- Evidence-based reviews are expensive, time consuming, and highly selective in what they cover. ODS needs to assess the quantity of the evidence available before deciding to sponsor an evidence report. For areas in which few data are available, the cost of a report might not justify the result.
- ODS must carefully construct the questions to be addressed in the evidence-based review to ensure that the report will provide useful answers. Content experts who will use the final report, ODS staff, and AHRQ experts should be involved in constructing questions.
- The questions should be defined and the appropriate literature base should be identified before ODS submits the questions to AHRQ for inclusion in a statement of work.
- Once the draft questions have been developed, appropriate NIH ICs should be invited to participate in developing the evidence-based reviews. ODS should request IC participation directly from the IC directors to ensure support for the process and maximize the likelihood that the report will be useful.
- ODS and IC staff, with as many technical expert panel members as possible, should actively participate in the technical expert panel conference calls.
- ODS, AHRQ, and the relevant IC staff should review and approve of all changes to the original questions, study types, or literature scope made by the technical expert panel or Evidence-based Practice Center.
- Literature reviews should not be incorporated into the evidence-based review synthesis.

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[8] NIH State-of-the-Science Conference Statement on Multivitamin/Mineral Supplements and Chronic Disease Prevention. Ann Intern Med 2006; 145:364–371 (available at http://consensus.nih.gov/2006/2006MultivitaminMineralSOS028main.htm).

[9] Cranney A, Horsley T, O'Donnell S, Weiler H, Puil L, Ooi D, et al. Effectiveness and safety of vitamin D in relation to bone health. Evidence Report/Technology Assessment No. 158 (prepared by the University of Ottawa Evidence-based Practice center [UO-EPC] under Contract No. 290-02-0021). AHRQ Publication No. 07-E013. Rockville, MD: AHRQ, August 2007.

Plans for the Future. Evidence-based reviews have provided important information on the scope of research needed for specific dietary supplements. Additional dietary supplements could become topics for such reviews. However, ODS has also identified certain questions about the role of evidence-based reviews in nutrition research that need to be addressed before ODS sponsors additional reviews. ODS has issued a contract to the Tufts Evidence-based Practice Center to identify ways to better adapt evidence-based reviews to the evaluation of nutritional research topics.

Additional Information on the Evidence-based Review Program

- The Web site for NIH State-of-the-Science Conference on Multivitamin/Mineral Supplements and Chronic Disease Prevention, which took place on May 15-17, 2006, is at http://consensus.nih.gov/2006/2006MultivitaminMineralSOS028main.htm.
- A list of evidence-based reviews on dietary supplements carried out by the AHRQ Evidence-based Practice Centers with ODS support is in Appendix I.

Section Three: Communications

The ODS mission stresses the dissemination of research results and education of the public as ways to enhance the quality of life and health of the U.S. population. To fulfill this mission, Goal 5 of the ODS 2004-2009 strategic plan is to expand and conduct outreach activities that inform and educate the public, health care providers, and scientists about the benefits and risks of dietary supplements.

ODS has made significant advances in improving its communications, outreach, and education on dietary supplements through four programs:

- Communications Program
- IBIDS database program
- CARDS database program
- Federal Dietary Supplement Working Group

ODS developed IBIDS and CARDS in response to language in the DSHEA. ODS formed the Federal Dietary Supplement Working Group in 2005 to ensure structured communication with other Federal agencies with an interest in dietary supplements. The Communications Program budget includes contracts that account for less than 1% of the ODS budget.

I. Communications

Scope of the Program. The ODS Communications Program leads ODS's development and dissemination of science-based information about dietary supplements. The goals of the program are to promote public understanding of the role of nutrition and dietary supplements in maintaining health and to inform and educate health care providers and scientists about the benefits and risks of dietary supplements.

Progress. The Communications Program has developed information products and resources on dietary supplements. An external evaluation of the program in 2005 helped refocus the office's efforts. The following components reflect the results of this evaluation.

ODS Web site. The ODS Web site (http://ods.od.nih.gov) has become ODS's key vehicle for disseminating information to the public. The Web site provides information on dietary supplements to a broad audience, including researchers, health care providers, and the general public. ODS launched its current Web site in 2004, and ongoing evaluations of Web site use have led to additional enhancements. ODS plans to release a new version of the Web site in the near future to improve usability further.

Fact sheets on dietary supplements. ODS has developed and maintained fact sheets that provide comprehensive information on dietary supplement ingredients for health professionals. The fact sheets are available on the ODS Web site. ODS is developing two new versions: one version targeted to consumers and a second version that is short (one two-sided page) and easy to read.

*Newsletter***.** The ODS newsletter, *ODS Update*, provides announcements about fact sheets, publications, databases, exhibits, conferences, workshops, and symposia. The newsletter also offers feature stories on current ODS projects and initiatives.

E-mail list. The ODS e-mail list distributes electronic copies of the newsletter and other news from ODS to researchers, clinicians, and members of the public interested in dietary supplement research.

IBIDS. See Section II below for details on IBIDS.

CARDS database. See Section III below for details on CARDS.

Annual Bibliography of Significant Advances in Dietary Supplement Research. This bibliography provides a snapshot of the scientific literature published in the previous year on dietary supplements. An international team of reviewers selects the abstracts to include. The most recent issue of the bibliography includes abstracts of 25 dietary supplement research papers published in 2007. Copies of all annual bibliographies are available on the ODS Web site.

Media inquiries. The Communications Program reorganized the ODS system for responding to inquiries from the media in 2005. A contractor now screens all media inquiries and only directs calls to a senior staff member when the call requires a specific area of expertise.

*Meeting coordination***.** Since 2006, the Communications Program has served as the coordinating center for all ODS-related meetings. Currently, the Communications Program is conducting outreach for meetings related to the ODS vitamin D initiative.

Exhibits program. In 2007, the Communications Program assumed responsibility for the ODS exhibits program. Communications staff members work with senior ODS staff to select the meetings at which ODS will exhibit each year.

Lessons Learned. Progress on the fact sheets has not been as rapid as desired. Several attempts to outsource some of the work have not been successful because the combination of skills required is difficult to find. However, ODS has managed many of its communications tasks effectively through contracts. Contracted tasks include:

- Web site redesign
- Web site user testing
- Evaluation of ODS research resources
- Outreach program development
- Fact sheets editing
- Glossary
- Professional administrative support
- Exhibits program

Plans for the Future. The Communications Program has identified a number of areas to develop in the future:

Glossary. The Communications Program is developing a glossary for use with the consumer fact sheets and the easy-to-read fact sheets. Hypertext links will be embedded in the glossary that point to the appropriate Web-based fact sheet.

ODS e-mail list. The ODS e-mail list is a useful means of communicating with an ever-expanding community of more than 3,500 people. The Communications Program plans to identify subgroups with shared interests so that it can send targeted messages only to interested groups.

Outreach partners. Program staff members have developed a comprehensive list of potential outreach partners, categorized by organization type (such as Federal, state, and local government; nonprofit and trade organizations; medical professional societies; advocacy organizations; media; and ODS staff contacts). A contractor is populating a database of descriptive information about these organizations, including mission, membership, activities, and contact information. This information will serve as the basis for the new ODS Web site and consumer fact sheet outreach plan.

Electronic newsletter. ODS plans to transition its print-formatted newsletter to an electronic newsletter. This format (headlines with a sentence or two of information hyperlinked to the full story) will allow ODS to send an increased amount of information more frequently to stakeholders because the production is more efficient. The electronic newsletter will be also be available on the ODS Web site.

Additional Information on the Communications Program

- Recent plans and surveys by the Communications Program are listed in Appendix J.

II. International Bibliographic Information on Dietary Supplements (IBIDS)

Scope of the Program. One of the activities that DSHEA mandated was to "collect and compile the results of scientific research relating to dietary supplements, including scientific data from foreign sources." ODS launched IBIDS in 1999 to address this mandate.

IBIDS is a database of published international scientific literature on dietary supplements that is publicly available on the ODS Web site. IBIDS helps researchers and the general public locate scientific literature on dietary supplements. Users can search through the more than 750,000 IBIDS records from multiple sources, including peer-reviewed journal articles from major medical, botanical, agricultural, chemical, and pharmaceutical databases. ODS developed and maintains IBIDS in collaboration with the Food and Nutrition Information Center of the USDA's National Agricultural Library.

Progress. IBIDS has continued to grow through the addition of citations on a quarterly basis; the continuous addition of new and unique journal collections; and updates and enhancements of special features, such as health outcomes and significant advances in dietary supplement research. Periodically, ODS has conducted user surveys to guide revisions and enhancements.

ODS launched a revised version of IBIDS in 2004. Some of the new features added at that time were:

- A display of the five most popular IBIDS searches
- The ability to view all article records in ODS's Annual Bibliography of Significant Advances in Dietary Supplement Research
- Embedded executable keyword search capability
- Images of botanicals and chemical formulae

In 2005, ODS added another feature to the database, IBIDS Health Outcomes. This feature presents articles of interest to consumers on certain health topics, such as the use of herbals for menopausal symptoms and omega-3 fatty acids for heart disease.

Since 2007, users have been able to search and access individual IBIDS database records using Google.

ODS also developed IBIDS Clinical, a specialized subset of IBIDS geared to clinical practitioners and researchers, in response to the 2004 review's identification of an unmet need for information on dietary supplements for clinicians. In its development phase, IBIDS Clinical currently contains information on 11 dietary supplements.

Lessons Learned. As with any Web-based product, IBIDS requires continual modifications and updating to remain current and reflective of recent research. This places increasing demands on staff to maintain the database at a time when they are also pilot testing and evaluating new features. The availability of staff support for this project has varied over the years, causing delays and setbacks in meeting stated goals. The IBIDS team members have increased their ability to cope with changes in information technology support staff and have learned some of the information technology functions needed to maintain IBIDS functionality.

Like the ODS fact sheet pages, the IBIDS page has consistently been one of the top five most frequently visited pages on the ODS Web site. ODS opened IBIDS to Google in March 2007 and the number of monthly citations for IBIDS increased to an all-time record high.

Plans for the Future. ODS is developing and pilot testing IBIDS Clinical. This new feature will include article records drawn from the full IBIDS database that are relevant to the use of dietary supplement products by people. IBIDS Clinical will classify these records by supplement(s) being tested and evidence level or study design.

ODS is also adding a free-text search feature that will allow users to search across and within data on supplements for health outcomes and other terms of interest. ODS plans to test the usability of and collect user input on this feature.

Additional Information on the IBIDS Program

- IBIDS is available at http://ods.od.nih.gov/Health_Information/IBIDS.aspx.
- Information on activities to enhance IBIDS is in Appendix K.

III. Computer Access to Research on Dietary Supplements (CARDS)

Scope of the Program. One of the activities mandated by DSHEA was to "compile a database of scientific research on dietary supplements and individual nutrients." In response, ODS developed CARDS, a database of federally funded research projects pertaining to dietary supplements. CARDS is user friendly, searchable, and publicly available through the ODS Web site.

Progress. Currently, CARDS contains data on projects funded since 1999 by the USDA, DoD, and NIH ICs. ODS will add projects funded by other Federal agencies to CARDS as they become available. CARDS contains more than 7,500 records.

CARDS builds on records from the Human Nutrition Research and Information Management system. This Federal government-wide, online database was created for fiscal accounting, management, and control of cross-agency nutrition research activities. Because CARDS has a narrower focus than the Human Nutrition Research and Information Management system, CARDS can provide more details on each research project.

CARDS provides information for researchers, health care providers, industry, and the general public. Because CARDS includes budget information, it is also useful to Congress, Federal agencies, and NIH ICs.

Codes assigned to each research project allow CARDS users to identify:

- Research related to specific dietary supplement ingredients
- Type of study, such as clinical trial phase or whether the study includes animals
- Health outcomes or biological effects
- Whether the research is directly or indirectly related to dietary supplements.

Lessons Learned. It has taken time to gather dietary supplement research data from the multiple NIH ICs as well as other Federal agencies. Encouraging coders in these various Federal programs to use the Human Nutrition Research and Information Management Codes 36 and 37 to classify their dietary supplement-related research requires ongoing review and communication. Identifying contacts from whom to collect information at many Federal agencies continues to be a challenge. CARDS now contains more than 7,500 records collected over 7 years. This database will become increasingly useful in detecting trends in the Federal funding of dietary supplement research.

Plans for the Future. ODS plans to expand coverage of dietary supplement research in CARDS to include projects supported by other Federal agencies, such as the National Aeronautics and Space Agency, Department of Veterans Affairs, and FDA. In addition, ODS plans to use CARDS to analyze trends in dietary supplement research funding and as a reference source for Federal funding of dietary supplement research. ODS plans to write an article providing an update on trends in dietary supplement research.

Additional Information on the CARDS Program

- CARDS is available at http://ods.od.nih.gov/Research/CARDS_Database.aspx.
- Detailed information on the history of CARDS records is in Appendix L.

IV. Federal Dietary Supplement Working Group

Scope of the Program. The DSHEA specified that ODS was to serve as "the principal advisor to the Secretary [of DHHS] and to the Assistant Secretary for Health and provide advice to the Director of the National Institutes of Health, the Director of the Centers for Disease Control and Prevention, and the Commissioner of Food and Drugs [of the FDA] on issues relating to dietary supplements." To fulfill these responsibilities, ODS established a working group of public and private scientists to facilitate communication on dietary supplement issues. However, this ad hoc group never became functionally useful. With the revision of the strategic plan in 2004, a more formal Federal Dietary Supplement Working Group was established.

Progress. The Federal Dietary Supplement Working Group has allowed ODS to implement one of the five principal goals in the ODS 2004-2009 Strategic Plan, "expanding and conducting outreach efforts that inform and educate" through various means, including serving "as a key informational resource to DHHS and other Federal agencies on issues related to dietary supplements." The working group meets twice a year to maintain communications between ODS and its Federal partners. The current group has approximately 45 members. Most come from the NIH ICs and relevant offices, as well as the FDA, CDC, DHHS Office of Disease Prevention and Health Promotion, AHRQ, NIST, U.S. Army Research Institute of Environmental Medicine, and USDA.

Lessons Learned. The formal presentations and candid discussions at each meeting and the informal conversations that result from member relationships facilitated by the working group ensure that each partner is aware of each other's activities. Members are also familiar with the challenges faced by all member agencies with respect to dietary supplement research, regulations, controversies, product quality, and related matters. The meetings are especially important for ensuring that ODS remains at the center of all dietary-supplement research, education, and regulation-related issues addressed throughout the Federal government. The Federal Working Group has become an important means for ODS to build bridges and establish partnerships for addressing emerging and continuing scientific issues related to dietary supplements.

Plans for the Future. ODS will continue to coordinate twice-yearly meetings of the Federal Dietary Supplement Working Group.

Additional Information on the Federal Dietary Supplement Working Group

- The list of Federal Dietary Supplement Working Group members is in Appendix M.

Section Four: Science and Policy Interactions

The DSHEA made ODS the principal Federal advisor on issues relating to dietary supplements, including dietary intake regulations, the safety of dietary supplements, and health claims about dietary supplements. Some of the scientific issues that arise with respect to dietary supplements involve ongoing public policy discussions. This section presents three examples of current ODS collaborations to collect information on scientific issues that is needed for policy discussions:

- **Vitamin D Initiative**. ODS is coordinating the NIH vitamin D initiative to promote research exploring newly appreciated roles of vitamin D in human health.
- **Use of Dietary Supplements by Military Personnel**. ODS is a member of the DoD Dietary Supplement Committee that oversees dietary supplement use by military personnel.
- **Nutrient Intake Reference Values**. ODS has provided financial support for conferences and workshops on nutrient intake reference values, especially values for vitamins and minerals found in dietary supplements. In addition, ODS staff have actively collaborated in ongoing efforts to evaluate these reference values.

No single program at ODS is responsible for coordinating policy-related activities. Instead, ODS staff scientists work with other national and international organizations to address policy issues related to the ODS mandate. Staff time accounts for most of the cost of these interactions.

I. Vitamin D Initiative

Scope of the Program. Vitamin D is a unique nutrient in that it is available through both endogenous production from sun exposure and from foods and dietary supplements. Accumulating evidence indicates that in addition to calcium metabolism, vitamin D contributes to immune function and inflammation reduction. This nutrient also has effects on cell proliferation and differentiation and on programmed cell death. ODS is playing an active role in coordinating research on vitamin D to inform ongoing evaluations of the recommended daily intake of vitamin D.

Progress. ODS and NICHD cosponsored a two-day conference, Vitamin D and Health in the 21st Century: Bone and Beyond, on October 9-10, 2003. The conference included discussions of the measurement and maintenance of vitamin D status and the development of programs to reduce the prevalence of vitamin D insufficiency. Conference participants identified a number of research needs.

ODS has pursued several collaborations with other agencies to address some of the research needs identified during the 2003 conference:

- A contract with NIST to develop reference materials for measuring vitamin D in serum
- Support for a vitamin D food analysis and composition database developed by the USDA with additional support from NIST, the FDA, and the Beverage Institute for Health and Wellness (sponsored by the Coca Cola Company)
- Support of NHANES to include the determination of parathyroid hormone and vitamin D status across the life cycle

- Support for an AHRQ evidenced-based review of vitamin D and health.

ODS cosponsored a second NIH conference on vitamin D and health in the 21st century in 2007. This conference addressed the findings of the AHRQ evidence-based review on vitamin D and identified future research needs. More than 450 participants from the scientific, health care, and dietary supplement industry communities attended this conference. Immediately following the conference, ODS organized an interdisciplinary roundtable discussion to establish the framework for a vitamin D research agenda. The *American Journal for Clinical Nutrition* published the conference and roundtable proceedings.[10] In addition, ODS presented the results of the conference in a symposium, Vitamin D and Health in the 21st Century: Research Needs and Tools for Researchers, in during Experimental Biology 2008.

ODS also established the Vitamin D Federal Working Group to promote and move forward the research agenda developed during the symposium. This working group brings NIH IC representatives together to identify NIH-wide initiatives for further research on the role of vitamin D in human health.

Lessons Learned. The evidence-based review on vitamin D provided a well-grounded and strong framework for the second conference and roundtable. The identification of research needs by an impartial, interdisciplinary roundtable of experts has proven to be extremely valuable. The roundtable discussion reinforced the findings from the evidence-based review. Both the roundtable participants and the review's authors concluded that the evidence on the relationship between biomarkers of vitamin D exposure and functional outcomes is insufficient, except in the elderly.

The NIH conferences on vitamin D have given ODS valuable opportunities to frame research directions and work with several NIH ICs. ODS has formalized its partnership with NIH ICs through the Vitamin D Federal Working Group.

ODS has revised and updated its Web-based fact sheet on Vitamin D to reflect emerging knowledge.

A new, more rapid and validated assay for determining the vitamin D and 25-hydroxyvitamin D content in foods and supplements is needed.

Plans for the Future. ODS is well positioned to continue leading the establishment of an evidence-based research agenda for vitamin D through the Vitamin D Federal Working Group.

Additional Information on the Vitamin D Initiative

- A list of workshops and reports associated with the Vitamin D initiative is in Appendix N.

II. Use of Dietary Supplements by Military Personnel

[10] Vitamin D and health in the 21st century: an update. Am J Clin Nutr. 2008; 8:483S-592S.

Scope of the Program. Some unique challenges exist in advancing research on the use of dietary supplements by healthy population groups because NIH does not typically award investigator-initiated grants for studies in healthy populations. ODS has had a long and active interest in this area since its first 1996 conference, Role of Dietary Supplements for Physically Active People, and its 2002 symposium, Science and Policy of Performance-enhancing Products. In 2005, ODS joined the DoD Dietary Supplement Committee, which meets twice a year. The DoD clinicians and dietitians from across the services and representatives of other Federal agencies, such as ODS and FDA, on this committee discuss emerging topics related to supplement use and safety for troops at home or in deployment.

Progress. In 2005, ODS partnered with the Natural Marketing Institute to fund a survey of supplement use-related behavioral patterns in military personnel. The survey results showed that 71% of the U.S. military population living off-base was using dietary supplements; this rate is similar to that of the non-military population (73%). However, larger percentages of military personnel were using sports nutrition and weight loss supplements than non-military personnel. The military personnel who consumed supplements tended to be older and were more likely to have postgraduate education than military personnel who did not consume supplements frequently.

In 2006, the Samueli Institute invited ODS to serve on an oversight committee. The Samueli Institute was founded in 2001 and conducts research on biology and healing in alternative, complementary, integrative, and traditional medical practices. The Samueli Institute received congressional funding for its Military Research Program–Metabolic Defense, which studies the use of dietary and nutritional supplements by military personnel. ODS and DoD representatives review research projects under consideration for funding by this program.

Also in 2006, ODS served as a reviewer for the Biobehavioral Performance Science and Technology Programs at Brooks Air Force Base at the request of DoD and the American Institute of Biological Sciences. ODS prepared and submitted written comments on the programs under consideration.

ODS supported the development of the Institute of Medicine's report, *Use of Dietary Supplements by Military Personnel,* published in 2008.[11] This report originated with a request from the Military Nutrition Division of the U.S. Army Research Institute of Environmental Medicine to the Institute of Medicine for the Food and Nutrition Board's Committee on Military Nutrition Research to evaluate dietary supplement use by military personnel. ODS provided funding for the workshop that produced the final report.

Lessons Learned. The DoD's interest in dietary supplement use by military personnel has led to programs that can address the safety of dietary supplement use by healthy people. ODS has served as a partner in that effort.

[11] Committee on Dietary Supplement Use by Military Personnel, Institute of Medicine. Use of Dietary Supplements by Military Personnel. Washington, DC: The National Academies Press, 2008.

Plans for the Future. The Institute of Medicine's evaluation of dietary supplement use in the military will provide a framework for future investigations with the DoD on the use of dietary supplements in healthy populations.

Additional Information for Use of Dietary Supplements by Military Personnel

- Publications and presentations related to the use of dietary supplements by military personnel can be found in Appendix O.

III. Nutrient Intake Reference Values

Scope of the Program. The Dietary Reference Intakes (DRIs) are a set of reference values developed by the Institute of Medicine's Food and Nutrition Board for nutrient intakes for healthy persons in the United States and Canada. The DRIs provide a basis for several nutrition-related initiatives, including developing nutrient-related Federal and state policies, monitoring the nutritional status of U.S. population groups, identifying research needs, planning and evaluating research studies, and assisting health professionals in patient counseling and consumer education. ODS supports and participates in several key national and international efforts to model and assess DRIs for dietary supplements.

Progress. ODS provided financial support for the scientific workshop on nutrient risk assessment organized by the United Nations' Food and Agriculture Organization and the World Health Organization in May 2005. The workshop produced a global model for establishing upper levels of intake for nutrients and related substances. The workshop sponsors published this model in 2006. The workshop introduced systematic review processes into nutrient risk assessments. An international scientific conference, Biomarkers of Effect, is being planned as a follow-up.

ODS supported an evaluation by the AHRQ Evidence-based Review Center at Tufts University to evaluate how best to integrate evidence-based reviews into the processes for determining nutrient reference values.

ODS provided funding for and participated in the Institute of Medicine's Food and Nutrition Board workshop, The Development of DRIs 1994–2004: Lessons Learned and New Challenges, in September 2007. This workshop brought together representatives from the U.S. and Canadian governments, nutritionists and research scientists from universities and industry, and members of previous DRI study committees.

ODS supports the joint U.S. and Canadian effort to review the vitamin D and calcium DRIs established in1997. This review will use the lessons learned from the 2007 Institute of Medicine conference and the September 2007 vitamin D conference sponsored by ODS and the National Cancer Institute, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, and the American Society for Nutrition.

Lessons Learned. Broad collaborations are essential for modeling and assessing nutrient reference values. The integration of evidence-based reviews and systematic risk assessment

approaches is key to improving the scientific rigor, usefulness, and transparency of future DRI reviews.

Plans for the Future. The Institute of Medicine's Food and Nutrition Board is working with the U.S. and Canadian working group to identify criteria that will provide a sufficient basis to initiate future reviews of DRIs. ODS will continue to participate in this working group.

Additional Information for Nutrient Intake Reference Values

- Publications relevant to nutrient intake reference values with ODS staff as coauthors are listed in Appendix P.

APPENDICES

Appendix A: Goals and Initiatives from the ODS Strategic Plan for 2004 - 2009

The five original statements of goals have been retained as the charge for ODS programs in 2004-2009. They emphasize research (the first four) and information communication and education (the fifth). They maintain continuity in the ODS mission and purpose over a 10-year span. Some changes in wording have been incorporated to reflect progress toward these goals; identification of emerging needs; and development of new techniques, approaches, and opportunities.

The initiatives associated with goals 1 and 2 identify research needs and opportunities that may involve similar or related experimental or clinical approaches. However, the two goals and their respective initiatives are listed separately because the purpose of each initiative and the experimental and clinical endpoints are specific to each goal. In addition, initiatives within the other goals that are related to goals 1 and 2 are identified by an asterisk (*).

ODS Goals for Research, Education, and Information Communication: 2004-2009

- Goal 1: Expand the evaluation of the role of dietary supplements in disease prevention and in reduction of risk factors associated with disease.
- Goal 2: Foster research that evaluates the role of dietary supplements in maintaining and improving optimal physical and mental health and performance.
- Goal 3: Stimulate and support research to further understanding of the biochemical and cellular effects of dietary supplements on biological systems and their physiological impact across the life cycle.
- Goal 4: Promote and support the development and improvement of methodologies appropriate to the scientific study of dietary supplement ingredients.
- Goal 5: Expand and conduct outreach activities that inform and educate the public, health care providers, and scientists about the benefits and risks of dietary supplements.

Goal 1: Expand the evaluation of the role of dietary supplements in disease prevention and in reduction of risk factors associated with disease.

- Expand research that advances assessment of the potential roles of dietary supplements in disease prevention and risk reduction as identified in DSHEA and in the original ODS strategic plan.
- Stimulate and support evidence-based evaluations of the role of dietary supplements, including evaluation of the safety and efficacy of supplement use in the prevention and reduction of risks for chronic diseases.
- Place greater emphasis on identifying opportunities for NIH interdisciplinary research on dietary supplements where interests and opportunities exist in the programmatic goals of

several NIH ICs. For example, collaborate with ICs in clinical trials designed to evaluate the role of dietary supplements in disease prevention and risk reduction, with due regard for safety and efficacy as appropriate.
- Encourage investigators submitting research applications to NIH in response to initiatives to include studies that can add to the knowledge base concerning the roles of dietary supplements in various disease states.
- Expand the cadre of research scientists qualified by training and career development to undertake investigations on dietary supplements with particular emphasis on young investigators, minorities, and women, including those with expertise and interests in dietary supplements and those in related disciplines**.**
- Explore and foster new approaches to the study of dietary supplements in various activities and conditions resulting from disabilities and disease conditions.
- Foster research that focuses on beneficial and adverse interactions of dietary supplements with foods, drugs, and other dietary supplements in healthy persons and those with selected conditions where these interactions may affect disease prevention and risk reduction.

Goal 2: Foster research that evaluates the role of dietary supplements in maintaining and improving optimal physical and mental health and performance.

- Stimulate and support evidence-based evaluations of the role of dietary supplements in maintenance of optimal health, well-being, and physical and mental performance with appropriate attention to both safety and efficacy.
- Place greater emphasis on identifying opportunities for NIH interdisciplinary research on dietary supplements where interests and opportunities exist in the programmatic goals of several NIH ICs. For example, collaborate with ICs in clinical trials designed to test the role of dietary supplements in maintaining optimal health and performance including both beneficial and adverse effects where appropriate.
- Encourage investigators submitting research applications to NIH in response to initiatives to include studies that can add to the knowledge base concerning the beneficial and other effects of dietary supplements on optimal health and performance.
- Explore and foster new approaches to the study of dietary supplements in various activities and conditions consistent with optimal health, well-being, and physical and mental performance.
- Foster research that focuses on beneficial and adverse interactions of dietary supplements with foods, drugs, and other dietary supplements in healthy persons and those with selected diseases where these interactions may affect disease prevention and risk reduction.

Goal 3: Stimulate and support research to further understanding of the biochemical and cellular effects of dietary supplements on biological systems and their physiological impact across the life cycle.

- Stimulate additional research on how dietary supplements moderate, alter, or enhance metabolic, physiological, and psychological processes associated with maintenance or lack of optimal health and performance during the life cycle**.***

- Encourage greater collaboration on research within NIH on identifying and exploring the possible roles of dietary supplements and their bioactive ingredients on cellular, tissue, and organ metabolic changes that characterize various diseases and disorders and optimal health throughout the life cycle**.***
- Expand emphasis on the application of new and emerging technologies such as genomics and proteomics to identify specific actions of selected dietary supplements on subcellular and cellular systems as well as on tissues and organ systems in order to enhance knowledge of how these substances produce or influence harmful biochemical, physiological, and psychological effects**.***
- Explore approaches to the study of bioactive substances, particularly complex mixtures, that may help us to understand the mechanisms by which dietary supplements derived from plants and animals exert biological activities.

Goal 4: Promote and support the development and improvement of methodologies appropriate to the scientific study of dietary supplement ingredients.

- Support partnerships between dietary supplement research centers and interested ICs that will increase emphasis on chemical and biological characterization as well as biological effects of selected dietary supplement ingredients.
- Expand the development of valid, reliable analytical techniques for identifying specific dietary supplements and their bioactive ingredients to meet the needs of investigators studying the role of dietary supplements in health and disease.
- Produce and make available standardized reference materials appropriate for basic, preclinical, and clinical studies on the biological effects of dietary supplements in health and disease**.***
- Facilitate research on validation of the accuracy, sensitivity, and specificity of unique biomarkers of dietary supplement effects on known endpoints and their surrogates associated with specific chronic diseases, optimal health, and improved performance**.***
- Explore and develop guidelines on appropriate methods for determining the biological effects of dietary supplements in preclinical studies, including animal model systems, and clinical studies focused on efficacy or safety, including studies that address interactions with other ingested substances and lifestyle factors affecting health and disease development.*
- Stimulate further development and promote the use of paradigms for investigating the efficacy and safety of dietary supplements, including evidence-based evaluation of available information, standardized and known product composition, and appropriate preclinical studies as the basis for initiation of clinical trials**.***
- Expand emphasis on and continue to promote development of new and improved data collection techniques and epidemiological and survey methodologies that provide a valid, reliable scientific basis for identifying needs for analytical methods, determining the composition of dietary supplements, and determining patterns of dietary supplement use in various population groups identified by demographic factors.
- Collaborate with appropriate groups on surveys that assess dietary supplement use in order to estimate prevalence, frequency, duration, and type of use with the underlying goal of determining the relationships of usage patterns to health and disease risks.

- Improve measurement of dietary supplement and nutrient intakes and incorporate these improved measures into clinical studies to enhance the measurement of effects.

Goal 5: Expand and conduct outreach efforts that inform and educate the public, health care providers, and scientists about the benefits and risks of dietary supplements.

- Serve as a key informational resource to DHHS and other federal agencies on issues related to dietary supplements as stated in DSHEA**.***
- Promote the transfer and translation of information about dietary supplements from ODS to NIH and other federal agencies and encourage the use of this information by academia, industry, and other segments of the ODS constituency.
- Sponsor evidence-based reviews of the effectiveness and safety of dietary supplements and provide guidance to the scientific community, the media, and the public.
- Ensure that evidence-based scientific information is integrated into ODS health communications and education programs directed to the public at large.
- Encourage similar efforts with public- and private-sector partners(with particular attention to media representatives) to increase the availability of scientifically valid information critical to helping the public make decisions about the use of dietary supplements in health care.
- Increase the information available to health care providers and investigators in other disciplines to improve their understanding of and research on the roles of dietary supplements in health care delivery.
- Facilitate ease of access to ODS information and databases by all interested persons and organizations, with due regard for scientific peer review of validity and accuracy; educational, language, and cultural differences; and protection of privacy where appropriate. ODS anticipates that its efforts in this and related initiatives can be a model for the international ODS constituency.
- Assess public- and private-sector use of current ODS databases in order to enhance accessibility and utility of the information obtained.
- Improve ODS communication approaches to identify optimally effective tools and techniques for reaching the various segments of the ODS constituency and disseminating research findings to ODS public- and private-sector partners.

Appendix B: Research Grants Portfolio

Memo that ODS sent to NIH IC Directors requesting grants to cofund.

This memo serves to coordinate the ODS co-funding opportunities for both grants and conferences/workshops for FY 2008. The goals and initiatives are presented in the recently released ODS Strategic Plan 2004-2009 and emphasize the important role of ODS in research, education, and communication about dietary supplements (http://ods.od.nih.gov/pubs/strategicPlan.Final.pdf). These goals are summarized on page 3 of this memo.

The ODS entertains proposals for grant, intramural and conference co-funding on a quarterly basis. The table below describes the receipt, review, and notice of award dates for FY2008. Detailed instructions for submission of proposals are in this memo.

Reviews will take place according to the following schedule:

ODS Receipt Date – FY2008	**ODS Review Date**	**Notification of Funding to IC**
Oct. 29th	Nov. 14th	Nov. 28th
Jan. 14th	Jan. 23rd	Feb. 6th
April 28th (*revised)*	May 14th (*revised*)	May 28th (*revised*)
July 16th *(revised)*	July 30th	Aug. 8th

Primary consideration for support will be given to applications that deal with those dietary supplement ingredients or groups of supplements where current research is lacking or lagging, or where there is a likelihood of stimulating further research. Also, there may be dietary supplements where the data appear conflicting or where there is a need to clarify research gaps and opportunities as well as assess the balance between benefits and risks. Additionally, the office will seek to co-fund activities that target special population groups where additional science on supplements is needed. *Topics focusing on the use of supplements in reducing the risk of chronic disease are of keen interest to the ODS.*

Specific Guidance for Submission of Grants:

Support for grants, including supplemental projects, will vary depending on the mechanism, relevance to ODS mission, and proposed costs. Support generally ranges from $25,000 to $300,000. The ODS typically supports out-year funding for grants pending satisfactory progress and availability of funds.

Please e-mail the following materials:

- a copy of the e-summary statement and e-application
- a copy of the grant's abstract with a short critique highlighting the key points of the grant and relevance to ODS mission (1-2 pages)
- IC contact information.

Applications received without all of the above will be returned.

If you require an ODS decision by a particular date, please specify that and we will do all we can to accommodate your needs. If multiple grants are submitted for consideration, please prioritize your list. *We ask that all requests from your IC receive your approval prior to sending them to the ODS.*

A complete listing of ODS co-funded grants with abstracts is available on the ODS Web site: http://ods.od.nih.gov. A copy of the ODS co-funded grants for FY06 is also attached to this memo. You or your program staff are encouraged to contact us in ODS to discuss potential co-funding opportunities.

Specific Guidance for Submission of Intramural Funding Requests

Limited opportunities for intramural funding exist but will be capped at $100,000 (total costs) per award. Priority will be given to young scientists accepted into the NIH Intramural Tenure-Track Program and Senior Staff Fellows. All intramural funding requests must be documented by scientific review at the Division or higher level for consideration by ODS and accompanied by a memo describing the review process.

Proposals should be approximately 10 single-spaced pages in length (excluding investigator's c.v.'s and bibliography) providing rationale, background, study design including details on the study intervention, anticipated outcomes, proposed budget, and how this research is related to the ODS mission and goals. Please contact Dr. Rebecca Costello at costellb@od.nih.gov or 301-435-3605 to discuss your proposal idea prior to formal submission.

Specific Guidance for Submission of Conferences and Workshops:

A short description of the meeting(s) is necessary for the selection process. Please include: the tentative title; a brief summary of the purpose of the meeting; a general description, including the scope (national or international), size and format (workshop, small conference, symposium, forum, etc.); target audience; anticipated dates for the meeting, and possible outcomes (e.g., publications or proceedings); and budget information. A draft agenda with potential speakers and topics will be given higher priority. If similar symposia on the proposed topic have been held within the past two to three years, please describe how the currently proposed symposium will differ. If you are nominating an R13 Conference Grant for sponsorship; please include the grant application and summary statement, if available. ***Attachment A details the information to be submitted in a proposal request.***

If a conference or workshop is selected for sponsorship, the ODS will work closely with the program staff in your IC in the planning and development of this joint activity, with the goal of fostering a program and format that is productive and beneficial to program participants. Support for conferences, workshops, and symposia is typically in the range of $2,500 to $20,000, depending on the mechanism, focus, and level of ODS participation. ODS support is not intended to cover all expenses for a grant, conference or symposium. *We ask that all requests*

from your IC receive your approval prior to sending them to the ODS. You may e-mail your description to Rebecca Costello in ODS at costellb@od.nih.gov. You or your program staff are encouraged to contact us in ODS to discuss potential conference funding pportunities.

We appreciate your dissemination of this notice within your IC. Thank you for your assistance and continuing interest in ODS-sponsored programs. If you have any questions, please contact me at 301.435.2920 (phone) or by e-mail, coatesp@od.nih.gov.

Paul M. Coates, Ph.D.

Appendix C: Botanical Research Centers

Papers from the workshop on botanical supplements at Experimental Biology 2007 were published as a supplement, "The Science of Botanical Supplements for Human Health: A View from the NIH Botanical Research Centers," in the *American Journal of Clinical Nutrition* (2008;87:471S-513S).

The articles in this supplement are listed below.

Swanson CA, Liu Q-Y. Introduction to the National Institutes of Health Botanical Research Centers Program. Am J Clin Nutr. 2008;87:471S.

Ribnicky DM, Poulev P, Schmidt B, Cefalu WT, Raskin I. Evaluation of botanicals for improving human health. Am J Clin Nutr. 2008;87:472S-5S.

Barnes S, Birt DF, Cassileth BR, Cefalu WT, Chilton FH, Farnsworth NR, et al. Technologies and experimental approaches at the National Institutes of Health Botanical Research Centers. Am J Clin Nutr. 2008;87:476S-80S.

Cefalu WT, Ye J, Zuberi A, Ribnicky DM, Raskin I, Liu Z, et al. Botanicals and the metabolic syndrome Am J Clin Nutr. 2008;87:481S-7S.

Birt DF, Widrlechner MP, LaLone CA, Wu L, Bae J, Solco AKS, et al. Echinacea in infection. Am J Clin Nutr. 2008;87:488S-92S.

Weaver CM, Barnes S, Wyss JM, Kim H, Morré DM, Morré DJ, et al. Botanicals for age-related diseases: from field to practice. Am J Clin Nutr. 2008;87:493S-7S.

Chilton FH, Rudel LL, Parks JS, Arm JP, Seeds MC. Mechanisms by which botanical lipids affect inflammatory disorders. Am J Clin Nutr. 2008;87:498S-503S.

Farnsworth NR, Krause EC, Bolton JL, Pauli GF, van Breemen RB, Graham JG. The University of Illinois at Chicago/National Institutes of Health Center for Botanical Dietary Supplements Research for Women's Health: from plant to clinical use. Am J Clin Nutr. 2008;87:504S-8S.

van Breemen RB, Fong HHS, Farnsworth NR. Ensuring the safety of botanical dietary supplements. Am J Clin Nutr. 2008;87:509S-13S.

Appendix D: Training and Career Development

1. National Institutes of Health (NIH) career and training grants that received Office of Dietary Supplements (ODS) financial support in FY2008 are listed in Table C.1 below. Table C.2 provides descriptions of the career and training grant mechanisms used for programs cosponsored by ODS.

Table C.1: NIH Career and Training Grants Receiving ODS Financial Support, FY2008

Primary Institute or Center	Grant Number	Principal Investigator	Project Title
National Center for Complementary and Alternative Medicine	5F31AT003977-03	Emily Horvath, Indiana University–Purdue University at Indianapolis	Nutrient State & Cholesterol Dependent Action of Chromium
National Institute on Aging	5K23AG026768-03	Consuelo Wilkins, Washington University	Vitamin D in Older Adults: Cognition, Mood, and Hippocampal Volume
National Institute of Arthritis and Musculoskeletal and Skin Diseases	5K23AR052364-02	Diane L. Kamen, Medical University of South Carolina	The Role of Vitamin D in Systemic Lupus Erythematosus
National Institute of Child Health and Human Development (NICHD)	2K12HD043446-07	Eugene Oddone, Duke University	Building Interdisciplinary Careers/ Women's Health/ UC Davis (BIRCWH Training Grant)
NICHD	2K12HD043451-07	Jeannette Magnus, Tulane University	Tulane Building Interdisciplinary Research Careers in Women's Health (BIRCWH)
NICHD	5K12HD051958-04	Claire Pomeroy, University of California, Davis	Building Interdisciplinary Careers/ Women's Health/UC Davis (BIRCWH Grant)
NICHD	5T32HD007331-20	Kathleen Rasmussen, Cornell University	Training in Maternal and Child Nutrition
NICHD	5T32HD007445 - 15	William Heird, Baylor	Research Training in Maternal, Infant & Child Nutrition

Primary Institute or Center	Grant Number	Principal Investigator	Project Title
		College of Medicine	
National Heart, Lung, and Blood Institute (NHLBI)	5K23HL080231-03	Cynthia T. McEvoy, Oregon Health & Science Unviersity	In-Utero Smoke, Vitamin C, and Newborn Lung Function
NHLBI	5T32HL007918-10	Victora Darley-Usmar, University of Alabama, Birmingham	Training Program in Cardiovascular Pathophysiology

Note: Building Interdisciplinary Research Careers in Women's Health (BIRCWH), a program of the NIH office of Research on Women's Health, supports career development for junior faculty members who have recently completed clinical training or postdoctoral fellowships and who are starting basic, translation, clinical, or health services research relevant to women's health.

Table C.2: Career Development and Training Mechanisms Used by NIH Projects Cosponsored by ODS

Funding Mechanism	Description
F31	Individual predoctoral fellowship
T32	Institutional research training grant
K12	Mentored clinical scientist development program award
K23	Mentored clinical scientist development individual award

2. ODS Seminar Series, 2007–2008

Wednesday, October 3, 2007

Jack A. Yanovski, MD, PhD
Head, Unit on Growth and Obesity, Developmental Endocrinology Branch, National Institute of Child Health and Human Development, National Institutes of Health

Topic: Study of Supplemental Calcium in Overweight Out Patients (SCOOP): a randomized clinical trial of the effects of calcium supplementation on body weight and adiposity in overweight and obese adults

Wednesday, November 7, 2007

Joel B. Mason, MD
Scientist I and Director, Vitamins and Carcinogenesis Laboratory, Jean Mayer U.S. Department of Agriculture Human Nutrition Research Center on Aging at Tufts University

Topic: The schizophrenic vitamin: does folate prevent or promote colorectal cancer?

Wednesday, December 5, 2007

Alicia Carriquiry, PhD
Professor of Statistics, Iowa State University

Topic: Research strategies for assessing usual intakes of various population subgroups evaluated in the National Health and Nutrition Examination Survey (NHANES)

Wednesday, January 16, 2008

Emily Y. Chew, MD
Deputy Director, Division of Epidemiology and Clinical Research, National Eye Institute, National Institutes of Health

Topic: Nutritional therapies for age-related eye diseases

Wednesday, February 6, 2008

Jacob Selhub, PhD
Professor, Friedman School of Nutrition Science and Policy; Chief, Vitamin Metabolism Laboratory; and Senior Scientist, Jean Mayer USDA Human Nutrition Research Center on Aging, U.S. Department of Agriculture Human Nutrition Research Center on Aging at Tufts University

Topic: Folic acid intake and exacerbation of vitamin B12 deficiency

Wednesday, March 12, 2008

Kenneth Setchell, PhD
Professor of Pediatrics and Director, Clinical Mass Spectrometry Facility, University of Cincinnati College of Medicine

Topic: Fate and possible function of enantiomeric soy isoflavone metabolites

Wednesday, April 16, 2008

Helene McNulty, PhD

Professor of Human Nutrition & Dietetics, Northern Ireland Centre for Food and Health, School of Biomedical Sciences University of Ulster

Topic: Folic acid supplementation and optimal health: getting the balance right

Wednesday, May 7, 2008

Susan Mayne, PhD
Professor of Epidemiology and Public Health, Yale University School of Medicine

Topic: Controversies and solutions in epidemiologic studies of diet and cancer: what is diet and how do we measure it?

Appendix E: Conferences and Workshops

Recent publications from Office of Dietary Supplements conferences and workshops include:

Betz JM, Fisher KD, Saldanha LG, Coates PM. The NIH analytical methods and reference materials program for dietary supplements. *Anal Bioanal Chem.* 2007;389:19-25.

Brannon PM, Yetley EA, Bailey RL, Picciano MF. Summary of roundtable discussion on vitamin D research needs. *Am J Clin Nutr*. 2008 Aug;88(2):587S-592S.

Brannon PM, Yetley EA, Bailey RL, Picciano MF. Overview of the conference "Vitamin D and Health in the 21st Century: an Update". *Am J Clin Nutr*. 2008 Aug;88(2):483S-490S.

Coates PM, Chausmer A. Introduction to Conference on Psychoactive Botanical Products. *Pharmacol Therap.* 2004;102:97-8.

Coates PM, Thurn A, Dwyer JT. Introduction to State-of-the-Science Conference: Multivitamin/mineral supplements and chronic disease prevention. *Am J Clin Nutr*. 2007;85 (suppl):255S-256S.

Dwyer JT, Holden J, Andrews K, Roseland J, Zhao C, Schweitzer A, et al. Measuring vitamins and minerals in dietary supplements for nutrition studies in the USA. *Anal Bioanal Chem.* 2007;389:37-46.

Dwyer JT, Picciano MF, Betz JM, Coates PM. Mission and activities of the NIH Office of Dietary Supplements. *J Food Composition Analysis.* 2004;17:493-500.

Dwyer JT, Picciano MF, Betz JM, Fisher KD, Saldanha LG, Yetley EA, et al. Progress in developing analytical and label-based dietary supplement databases at the NIH Office of Dietary Supplements. *J Food Composition Analysis.* 2008;21:S83-S93.

Huang S-M, Hall, SD, Watkins P, Love LA, Serabjit-Singh C, Betz JM, et al. Drug interactions with herbal products and grapefruit juice: a conference report. *Clin Pharmacol Ther.* 2004;75:1-12.

London B, Albert C, Anderson ME, Giles WR, Van Wagoner DR, Balk E, et al. Omega-3 fatty acids and cardiac arrhythmias: prior studies and recommendations for future research: a report from the National Heart, Lung, and Blood Institute and Office Of Dietary Supplements Omega-3 Fatty Acids and their Role in Cardiac Arrhythmogenesis Workshop. *Circulation*. 2007 Sep 4;116(10):e320-35.

Purohit V, Russo D, Coates PM. Role of fatty liver, dietary fatty acid supplements, and obesity in the progression of alcoholic liver disease: introduction and summary of the symposium. *Alcohol.* 2004;34:3-8.

Raiten DJ, Picciano MF. Vitamin D and health in the 21st century: bone and beyond. Executive summary. *Am J Clin Nutr*. 2004 Dec;80(6 Suppl):1673S-7S.

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*. 2004;87:162-5.

Appendix F: Analytical Methods and Reference Materials

1. Recent publications by Office of Dietary Supplements (ODS) Analytical Methods and Reference Materials (AMRM) program staff:

Andrews KW, Schweitzer A, Zhao C, Holden JM, Roseland JM, Brandt M, et al. The caffeine contents of dietary supplements commonly purchased in the US: analysis of 53 products with caffeine-containing ingredients. Anal Bioanal Chem. 2007;389:231-9.

Betz JM, Fisher KD, Saldanha LG, Coates PM. The NIH analytical methods and reference materials program for dietary supplements. Anal Bioanal Chem. 2007;389:19-25.

Dwyer JT, Holden J, Andrews K, Roseland J, Zhao C, Schweitzer A, et al. Measuring vitamins and minerals in dietary supplements for nutrition studies in the USA. Anal Bioanal Chem. 2007;389:37-46.

Hildreth J, Hrabeta-Robinson E, Applequist W, Betz J, Miller J. Standard operating procedure for the collection and preparation of voucher plant specimens for use in the nutraceutical industry. Anal Bioanal Chem 2007;389(1):13-17.

Roman MC, Betz JM, Hildreth J. Determination of synephrine in bitter orange raw materials, extracts, and dietary supplements by liquid chromatography with ultraviolet detection: single-laboratory validation. J AOAC Int. 2007 Jan-Feb;90(1):68-81.

Rimmer CA, Howerton SB, Sharpless KE, Sander LC, Long SE, Murphy KE, et al. Characterization of a suite of ginkgo-containing standard reference materials. Anal Bioanal Chem. 2007 Sep;389(1):179-96.

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. 2004;87:162-5.

Sander LC, Putzbach K, Nelson BC, Rimmer CA, Bedner M, Thomas JB, et al. Certification of standard reference materials containing bitter orange. Anal Bioanal Chem. 2008 Jul;391(6):2023-34.

Schantz MM, Bedner M, Long SE, Molloy JL, Murphy KE, Porter BJ, et al. Development of saw palmetto (Serenoa repens) fruit and extract standard reference materials. Anal Bioanal Chem. 2008;392:427-38.

Sharpless KE, Anderson DL, Betz JM, Butler TA, Capar SG, Cheng J, et al. Preparation and characterization of a suite of ephedra-containing standard reference materials. J AOAC Int. 2006 Nov-Dec;89(6):1483-95.

Trucksess MW, Weaver CM, Oles CJ, Fry FS Jr, Noonan GO, Betz JM, et al. Determination of aflatoxins B1, B2, G1, and G2 and ochratoxin A in ginseng and ginger by multitoxin immunoaffinity column cleanup and liquid chromatographic quantitation: collaborative study. J AOAC Int. 2008 May-Jun;91(3):511-23.

Trucksess MW, Weaver CM, Oles CJ, Rump LV, White KD, Betz JM, et al. Use of multitoxin immunoaffinity columns for determination of aflatoxins and ochratoxin A in ginseng and ginger. J AOAC Int. 2007 Jul-Aug; 90(4):1042-9.

Whittaker P, Clarke JJ, San RH, Betz JM, Seifried HE, de Jager LS, et al. Evaluation of commercial kava extracts and kavalactone standards for mutagenicity and toxicity using the mammalian cell gene mutation assay in L5178Y mouse lymphoma cells. Food Chem Toxicol. 2008 Jan;46(1):168-74.

2. **Draft AMRM Web Site Menu**

Program Description

Standard Reference Materials® for Dietary Supplement Analysis

Dietary Supplements Quality Assurance Program

Analytical Methods for Dietary Supplements

Training, Education, Outreach

Funding Opportunities

Related Resources

AMRM Contacts

3. Selected material from the future AMRM Web site
   A. Standard Reference Materials® for Dietary Supplement Analysis (developed with ODS support)
      i. Matrix Standard Reference Materials Available from the National Institute of Standards and Technology (NIST)

- Bitter orange (*Citrus aurantium*): solid oral dosage form, extract, fruit. https://srmors.nist.gov/tables/view_table.cfm?table=110-9.htm
- Carrot extract in oil (carotenoids). https://srmors.nist.gov/tables/view_table.cfm?table=110-1.htm
- *Ephedra sinica*: aerial parts, commercial extract, native extract, protein powder, solid oral dosage form. https://srmors.nist.gov/tables/view_table.cfm?table=110-9.htm

- *Ginkgo biloba*: tablet, extract, leaves. https://srmors.nist.gov/tables/view_table.cfm?table=110-9.htm

ii.. Materials and Standards in Development by NIST

- Multivitamin/mineral (available soon)
- Omega-3 fatty acids in cod liver oil (available soon)
- Saw palmetto (*Serenoa repens*) (available soon)
- α-tocopherols
- Black cohosh (*Acteae racemosa*)
- Green tea (*Camellia sinensis*)
- Kudzu (*Pueraria lobata*)
- Omega-3 fatty acids in seed oils
- Red clover (*Trifolium pratense***)**
- Soy (*Glycine max*)
- St. John's wort (*Hypericum perforatum*)
- *Vaccinium* berries
- Vitamin D in serum
- Vitamins B6, B12 in serum

B. Dietary Supplements Quality Assurance Program

Since 2002, NIST's Analytical Chemistry Division of the Chemical Science and Technology Laboratory has been working with ODS and the Food and Drug Administration (FDA) Center for Food Safety and Applied Nutrition and Center for Drug Evaluation and Research to improve the quality of dietary supplements by producing Standard Reference Materials (SRMs) and developing analytical methods (http://www.cstl.nist.gov/programs/food.htm).

In 2007, NIST established the Dietary Supplements Quality Assurance Program (DSQAP) to improve the accuracy and precision of participants' measurements of nutrients, marker compounds, toxic elements, pesticides, or a combination of these factors in dietary supplement ingredients and finished products. DSQAP plans to conduct two or three exercises each year; participants in each exercise will analyze three to five samples.

Interest in the DSQAP has increased since the first comparison exercise in 2007. Thirty-four laboratories participated in a second comparison exercise in 2008. Study samples for this exercise included phytosterols in saw palmetto, flavonols in *Ginkgo biloba*, synephrine in bitter orange, arsenic in ephedra, and vitamins B_1 and B_2 in multivitamin/multielement tablets.

If you are interested in learning more about upcoming exercises or want to participate, (1) e-mail DSQAP@nist.gov or contact (2) Catherine Rimmer at (301) 975-3651 X3651 or catherine.rimmer@nist.gov or (3) Laura Wood at6 (301) 975-4111 or laura.wood@nist.gov.

C. Analytical Methods for Dietary Supplements

i. Published ODS-Supported Methods (not yet validated)

Joshi VC, Navarrete A, Khan IA. Authentication of *Valeriana procera* Kunth and comparative account of five Valeriana species. J AOAC Int. 2005 Nov-Dec;88(6):1621-5.

Navarrete A, Avula B, Choi YW, Khan IA. Chemical fingerprinting of *Valeriana* species: simultaneous determination of valerenic acids, flavonoids, and phenylpropanoids using liquid chromatography with ultraviolet detection. J AOAC Int. 2006 Jan-Feb;89(1):8-15.

Pullela SV, Choi YW, Khan SI, Khan IA. New acylated clionasterol glycosides from *Valeriana officinalis*. Planta Med. 2005 Oct;71(10):960-1.

Reich E, Schibli A, DeBatt A. Validation of high-performance thin-layer chromatographic methods for the identification of botanicals in a cGMP environment. J AOAC Int. 2008 Jan-Feb;91(1):13-20.

Verbitski SM, Gourdin GT, Ikenouye LM, McChesney JD, Hildreth J. Detection of *Actaea racemosa* adulteration by thin-layer chromatography and combined thin-layer chromatography-bioluminescence. J AOAC Int. 2008 Mar-Apr;91(2):268-75.

ii. Published ODS-Supported Single-Laboratory Validated (SLV) Methods

Croom E, Pace R, Paletti A, Sardone N, Gray D. Single-laboratory validation for the determination of terpene lactones in *Ginkgo biloba* dietary supplement crude materials and finished products by high-performance liquid chromatography with evaporative light-scattering detection. J AOAC Int. 2007 May-Jun;90(3):647-58.

Gray D, LeVanseler K, Pan M. Determination of flavonol aglycones in *Ginkgo biloba* dietary supplement crude materials and finished products by high-performance liquid chromatography: single laboratory validation. J AOAC Int. 2005 May-Jun;88(3):692-702.

Ji D, Roman M, Zhou J, Hildreth J. Determination of chondroitin sulfate content in raw materials and dietary supplements by high-performance liquid chromatography with ultraviolet detection after enzymatic hydrolysis: single-laboratory validation. J AOAC. 2007 May-Jun;90(3):659-69.

Müller A, Pietsch B, Faccin N, Schierle J. Method for the determination of lycopene in supplements and raw material by reverse-phase liquid chromatography: single laboratory validation. J AOAC Int. 2008 Nov-Dec;91(6):in press.

Orozco D, Skamarack J, Reins K, et al. Determination of ubidecarenone (Coenzyme Q10, ubiquinol-10) in raw materials and dietary supplements by high-performance liquid chromatography with ultraviolet detection: single-laboratory validation. J AOAC Int. 2007 Sep-Oct;90(5):1227-36.

Roman MC, Betz JM, Hildreth J. Determination of synephrine in bitter orange raw materials, extracts, and dietary supplements by liquid chromatography with ultraviolet detection: single-laboratory validation. J AOAC Int. 2007 Jan-Feb;90(1):68-81.

Schierle J, Pietsch B, Ceresa A, Fizet C, Waysek EH. Method for the determination of β-carotene in supplements and raw materials by reversed-phase liquid chromatography: single laboratory validation. J AOAC Int. 2004 Sep-Oct;87(5):1070-82.

Sorenson W, Sullivan D. Determination of campesterol, stigmasterol, and beta-sitosterol in Saw Palmetto raw materials and dietary supplements by gas chromatography: single-laboratory validation. J AOAC Int. 2006 Jan-Feb;89(1):22-34.

Sullivan D, Wehrmann J, Schmitz J, Crowley R, Eberhard J. Determination of ephedra alkaloids by liquid chromatography/tandem mass spectrometry. J AOAC Int. 2003 May-Jun;86(3):471-5.

Tang WT, Wong SK, Law TY, Pang KC, Sin D, Tam YK. Method for the determination of aconitum alkaloids in dietary supplements and raw materials by reversed-phase liquid chromatography with ultraviolet detection and confirmation by tandem mass spectrometry: single-laboratory validation. J AOAC Int. 2006 Nov-Dec;89(6):1496-514.

Trucksess M, Weaver C, Oles C, D'Ovidio K, Rader J. Determination of aflatoxins and ochratoxin A in Ginseng and other botanical roots by immunoaffinity column cleanup and liquid chromatography with fluorescence detection. J AOAC Int. 2006 May-Jun;89(3):624-30.

Trujillo WA, Sorenson WR, La Luzerne P, Austad JW, Sullivan D. Determination of aristolochic acid in botanicals and dietary supplements by liquid chromatography with ultraviolet detection and by liquid chromatography/mass spectrometry: single laboratory validation confirmation. J AOAC Int. 2006 Aug;89(4):949-59.

Zhou JZ, Waszkuc T, Mohammed F. Single laboratory validation of a method for determination of glucosamine in raw materials and dietary supplements containing glucosamine sulfate and/or glucosamine hydrochloride by high-performance liquid chromatography with FMOC-Su derivatization. J AOAC Int. 2004 Sep-Oct;87(5):1083-92.

iii. Published ODS-Supported Collaborative Study Validated Methods

Brown PN, Roman MC. Determination of hydrastine and berberine in goldenseal raw materials, extracts and dietary supplements by high-performance liquid chromatography with UV: collaborative study. J AOAC Int. 2008 Jul-Aug;91(4):694-701.*

Collison M. Determination of total soy isoflavones in dietary supplements, supplement ingredients, and soy foods by high-performance liquid chromatography with ultraviolet detection: collaborative study. J AOAC Int. Forthcoming 2008 Sep-Oct;91(5).*

Deshpande J, Austad J, Schierle J, Waysek EH. Determination of lycopene in dietary supplements and raw materials by high-performance liquid chromatography: collaborative study. J AOAC Int. Forthcoming 2008 Nov-Dec;91(6).

Gray D, LeVanseler K, Pan M, Waysek EH. Evaluation of a method to determine flavonol aglycones in Ginkgo biloba dietary supplement crude materials and finished products by high-performance liquid chromatography: collaborative study. J AOAC Int. 2007 Jan-Feb;90(1):43-53.*

Ji D, Roman M. Determination of chondroitin sulfate content in raw materials and dietary supplements by high-performance liquid chromatography with UV after enzymatic hydrolysis: collaborative study. J AOAC Int. Forthcoming 2008 Nov-Dec;91(6).

Lunetta S, Roman M. Determination of Coenzyme Q10 content in raw materials and dietary supplements by high-performance liquid chromatography-UV: collaborative study. J AOAC Int. 2008Nov-Dec;91(6):702-8.

Roman MC. Determination of ephedra alkaloids in urine and plasma by high-performance liquid chromatography with UV: collaborative study. J AOAC Int. 2004 Jan-Feb;87(1):15-24.

Roman MC. Determination of ephedrine alkaloids in botanicals and dietary supplements by high-performance liquid chromatography with UV: collaborative study. J AOAC Int. 2004 Jan-Feb;87(1):1-14.*

Roman M, Benjamin RL. Determination of dimethylsulfoxide (DMSO) in methylsulfonylmethane (MSM) raw materials by GC-FID: collaborative study. J AOAC Int. Forthcoming 2008 Nov-Dec;91(6).

Roman M, Benjamin RL. Determination of methylsulfonylmethane (MSM) content in raw materials and dietary supplements by GC-FID: collaborative study. J AOAC Int. Forthcoming 2008 Nov-Dec;91(6).

Sorenson WR, Sullivan D. Determination of aristolochic acid I in botanicals and dietary supplements potentially contaminated with aristolochic acid I using LC-UV with confirmation by LC/MS: collaborative study. J AOAC Int. 2007 Jul-Aug;90(4):925-33.*

Sorenson WR, Sullivan D. Determination of campesterol, stigmasterol, and beta-sitosterol in saw palmetto raw materials and dietary supplements by gas chromatography: collaborative study. J AOAC Int. 2007 May-Jun;90(3):670-8.*

Szpylka J, DeVries JW. Determination of β-carotene in supplements and raw materials by reversed-phase high pressure liquid chromatography: collaborative study. J AOAC Int. 2005 Sept-Oct;88(5):1279-91.*

Trucksess MW, Weaver CM, Oles CJ, Fry FS Jr, Noonan GO, Betz JM, et al. Determination of aflatoxins B1, B2, G1 and G2 and ochratoxin A in ginseng and ginger by multitoxin immunoaffinity column cleanup and liquid chromatographic quantitation: collaborative study. J AOAC Int. 2008 May-Jun;91(3):511-23.*

Trujillo WA, Sorenson WR. Determination of ephedrine alkaloids in dietary supplements and botanicals by liquid chromatography/tandem mass spectrometry: interlaboratory study. J AOAC Int. 2003 July-Aug;86(4):657-68.

Trujillo WA, Sorenson WR. Determination of ephedrine alkaloids in human urine and plasma by liquid chromatography/tandem mass spectrometry: collaborative study. J AOAC Int. 2003 Jul-Aug;86(4):643-56.*

Wong SK. Determination of aconitum alkaloids in dietary supplements and raw botanical materials using LC-UV with confirmation by LC/MS: collaborative study. J AOAC Int. Forthcoming 2008 Nov-Dec;91(6).

Zhou JZQ, Waszkuc T, Mohammed F. Determination of glucosamine in raw materials and dietary supplements containing glucosamine sulfate and/or glucosamine hydrochloride by high-performance liquid chromatography with FMOC-Su derivatization: collaborative study. J AOAC Int. 2005 Jul-Aug;88(4):1048-58.*

*Approved as Official Methods of Analysis℠

iv. The following SLV studies of dietary supplement ingredients are currently in progress:
- Chondroitin sulfate SLV
- Green tea catechins SLV

Appendix G: Surveys of Dietary Supplement Use

Recent publications by ODS Dietary Surveys Program staff:

Dwyer J, Costello RB. Assessment of dietary supplement use. In: Coulston AM, Boushey CJ, editors. Nutrition in the prevention and treatment of disease, second edition. Burlington, MA: Academic Press, 2008:41-56.

Davis RE, Resnicow K, Atienza AA, Peterson KE, Domas A, Hunt A, et al. Use of signal detection methodology to identify subgroups of dietary supplement use in diverse populations. J Nutr. 2008 Jan;138(1):205S-211S.

Dwyer JT, Allison DB, Coates PM. Dietary supplements in weight reduction. J Am Dietet Assoc. 2005;105(Suppl):S80-6.

Dwyer JT, Costello RB. Assessment of dietary supplement use. In: Coulston AM, Boushey CJ, editors. Nutrition in the prevention and treatment of disease. 2nd edition. New York: Elsevier Press, 2008.

Dwyer J, Peterson J, Winters B, Liu W, Mitchell DC, Atkinson K. Do flavonoid intakes of postmenopausal women with breast cancer vary on very low fat diets? Nutr Cancer. 2008;60(4):450-60.

McDowell MA, Lacher DA, Pfeiffer CM, Mulinare J, Picciano MF, Rader JI, et al. Blood folate levels of the U.S. population: what the latest NHANES data show. NCHS Data Brief, No.2. Hyattsville, MD: National Center for Health Statistics, 2008. Available at http://www.cdc.gov/nchs/data/databriefs/db06.htm.

Morris MS, Picciano MF, Jacques PF, Selhub J. Plasma pyridoxal 5' -phosphate (PLP) in the United States population: the National Health and Nutrition Examination Survey, 2003-2004. Am J Clin Nutr. 2008;87(5):1446-54.

Pfeiffer CM, Johnson CL, Jain R, Yetley EA, Picciano MF, Rader J, et al. Trends in biochemical indices of folate and vitamin B12 status in the United States, 1988-2004. Am J Clin Nutr. 2007;86:718-27.

Pfeiffer CM, Osterloh JD, Kennedy-Stephenson J, Picciano MF, Yetley EA, Rader JI, et al. Trends in circulating concentrations of total homocysteine among US adolescents and adults: findings from the 1991-1994 and 1999-2004 National Health and Nutrition Examination Surveys. Clin Chem. 2008;54(5):801-13.

Picciano MF, Dwyer JT, Radimer KL, Wilcon DH, Fisher KD, Thomas PR, et al. Dietary supplement use among infants, children and adolescents in the United States 1999-2002. Arch Pediatr Adolesc Med. 2007;161:978-85.

Picciano MF, Yetley EA, Coates PM. Folate and health. Perspectives in agriculture, veterinary science, nutrition and natural resources. CAB Review 2007 Apr;2(0018).

Picciano MF, Yetley EA, Coates PM, McGuire MK. Update on folate and human health. Nutr Today. 2008, in press.

Potischman N, Cohen BE, Picciano MF. Dietary assessment in large epidemiological studies of maternal and child health: current status and research needs. J Nutr. 2006;136:686-9.

Radimer K, Bindewald B, Hughes B, Picciano MF. Dietary supplement use in adults in the US, 1999-2000. Am J Epidemiol. 2004;160:339-49.

Tamura T, Picciano MF. Folate and human reproduction. Am J Clin Nutr. 2006;83:993-1006.

Yaroch AL, Nebeling L, Thompson FE, Hurley TG, Hebert JR, Toobert DJ, et al. Baseline design elements and sample characteristics for seven sites participating in the Nutrition Working Group of the Behavior Change Consortium. J Nutr. 2008; 138(1):185S-92S.

Appendix H: Ingredient and Label-based Databases for Dietary Supplements

Recent publications from ODS Ingredient and Label-Based Databases for Dietary Supplements Program staff:

Andrews K, Roseland J, Zhao C, Schweitzer A, Holden JM, Perry C, et al. Commonly reported US adult multivitamin/mineral (MVM) products: analysis of labeled vs. analytical values for 19 vitamins and minerals. FASEB J. 2008;159:4.

Andrews KW, Schweitzer A, Zhao C, Holden JM, Roseland JM, Brandt M, et al. The caffeine contents of dietary supplements commonly purchased in the US: analysis of 53 products with caffeine-containing ingredients. Anal Bioanal Chem. 2007;339:231-40.

Dwyer JT, Holden J, Andrews K, Roseland J, Zhao C, Schweitzer A, et al. Measuring vitamins and minerals in dietary supplements for nutrition studies in the USA. Anal Bioanal Chem. 2007;339:37-46.

Dwyer JT, Picciano MF, Betz JM, Fisher KD, Saldanha LG, Yetley EA, et al. Progress in development of an integrated dietary supplement ingredient database at the NIH Office of Dietary Supplements. J Food Compost Anal. 2006;19:S108-14.

Roseland JM, Holden JM, Andrews KW, Zhao C, Schweitzer A, Harnly J, et al. Dietary supplement ingredient database (DSID): preliminary USDA studies on the composition of adult multivitamin/mineral supplements. J Food Comp and Analysis. 2008;21:S69-77.

Saldanha LG. US Food and Drug Administration regulations governing label claims for food products, including probiotics. Clin Infect Diseases 2008;6(Suppl 2):S119-21.

Yetley EA. Multivitamin and multimineral dietary supplements: definitions, characterization, bioavailability, and drug interactions. Am J Clin Nutr. 2007 Jan; 85(1):269S-76S.

Appendix I: Evidence-Based Reviews

1. The Evidence-based Practice Centers of the Agency for Healthcare Research Quality (AHRQ) have carried out the Office of Dietary Supplements (ODS)-supported evidence-based reviews on dietary supplements that are listed below. Additional information, with links to final reports from these reviews, is available on the AHRQ Web site, at http://www.ahrq.gov/clinic/epcix.htm.

   - B Vitamins and Berries and Age-Related Neurodegenerative Disorders (April 2006)
   - Health Effects of Omega-3 Fatty Acids on Arrhythmogenic Mechanisms in Animal and Isolated Organ/Cell Culture Studies (March 2004)
   - Health Effects of Omega-3 Fatty Acids on Lipids and Glycemic Control in Type II Diabetes and the Metabolic Syndrome and on Inflammatory Bowel Disease, Rheumatoid Arthritis, Renal Disease, Systemic Lupus Erythematosus and Osteoporosis (March 2004)
   - Multivitamin/Mineral Supplements and Prevention of Chronic Disease (May 2006)
   - Omega-3 Fatty Acids, Effects on Arrhythmogenic Mechanisms in Culture Studies (March 2004)
   - Omega-3 Fatty Acids, Effects on Asthma (March 2004)
   - Omega-3 Fatty Acids, Effects on Cancer (February 2005)
   - Omega-3 Fatty Acids, Effects on Cardiovascular Disease (March 2004)
   - Omega-3 Fatty Acids, Effects on Cardiovascular Risk Factors (March 2004)
   - Omega-3 Fatty Acids, Effects on Child & Maternal Health (August 2005)
   - Omega-3 Fatty Acids, Effects on Cognitive Functions (February 2005)
   - Omega-3 Fatty Acids, Effects on Eye Health (July 2005)
   - Omega-3 Fatty Acids, Effects on Mental Health (July 2005)
   - Omega-3 Fatty Acids, Effects on Organ Transplantation (February 2005)
   - Effects of Soy on Health Outcomes (August 2005)
   - Effectiveness and Safety of Vitamin D in Relation to Bone Health (August 2007)

2. The ODS Web site lists the journal articles published from the evidence-based reviews: http://ods.od.nih.gov/Research/Evidence-Based_Review_Program.aspx

3. Recent publications by ODS Evidence-based Review Program staff:

Balk EM, Horsley TA, Newberry SJ, Lichtenstein AH, Yetley EA, Schachter HM, et al. A collaborative effort to apply the evidence-based review process to the field of nutrition: challenges, benefits, and lessons learned. Am J Clin Nutr. 2007 Jun;85(6):1448-56.

Coates PM. Evidence-based reviews in support of health policy decisions. J Natl Cancer Inst. 2007 Jul 18;99(14):1059.

London B, Albert C, Anderson ME, Giles WR, Van Wagoner DR, Balk E, et. al. Omega-3 fatty acids and cardiac arrhythmias: prior studies and recommendations for future research. A report from the National Heart, Lung, and Blood Institute and Office of Dietary Supplements omega-3 fatty acids and their role in cardiac arrhythmogenesis workshop. Circulation. 2007;116(10):e320-35.

Appendix J: Communications

Recent plans and surveys of the Communications Program.

1. The Office of Dietary Supplements (ODS) developed and carried out its first proactive outreach plan for the May 2006 multivitamin and mineral conference. These outreach activities included:
    - Preparation of talking points for Paul Coates, Ph.D., Director of ODS, based on the panel statement from the conference
    - Radio media tour (in collaboration with the Office of Disease Prevention communications coordinator)
    - ODS e-mail list announcement
    - ODS newsletter article
    - Email notice to ODS trans-National Institutes of Health (NIH)/Agency Dietary Supplements Working Group
    - Coordination of publication of proceedings in *American Journal of Clinical Nutrition*
    - Mailings of *American Journal of Clinical Nutrition* proceedings to article authors, ODS Trans -NIH/Agency Working Group members, and media representatives.

2. ODS conducted a user survey on its Web site for 6 months (fall 2005 to spring 2006). Results included:
    - Two-thirds of users were women.
    - Fifty percent of users were members of the general public.
    - Ten percent of users were dietitians or nutritionists.
    - Nine percent of users were college or graduate students.
    - Sixty percent of users had a college degree.
    - Less than half of all users found the ODS Web site through a search engine.
    - The overall user satisfaction score of 80 (out of 100) put ODS's site in the top 20% of government Web sites. In comparison, the satisfaction score for the National Cancer Institute's cancer.gov site for the same time period was 81 and for MedLine Plus (a consumer-oriented Web site) was 85.

    Based on the results of usability testing in 2006 and 2007, ODS is redesigning its Web site. The office finished testing the new version in early spring 2008 and plans to make the site live by 2009. The updated version will include the following new features:
    - More powerful search engine
    - Reorganized content so that the home page focuses more on consumer information
    - Consumer versions of fact sheets

3. ODS communications staff members have implemented a plan and tracking system to keep the ODS fact sheets current. In October 2005 and December 2006, ODS contractors tested the usability of the ODS health professional and draft consumer fact sheets. Health

professionals who participated in the testing made it clear that they do not have time to read all of the information in the current versions of the fact sheets.

The test results showed that the 17 fact sheets currently available on the ODS Web site are written at a high reading level (12th grade plus). ODS is therefore rewriting the fact sheets to better serve health professionals. For each fact sheet, ODS will also produce two consumer versions:

- A basic version written at a lower reading level than the full health professional version.
- A two-page “quick facts “ version that is written at an intermediate reading level and is designed for both consumers and busy health professionals.

Appendix K: International Bibliographic Information on Dietary Supplements (IBIDS)

Activities to enhance IBIDS:

1. Update of IBIDS. As of mid-2008, the IBIDS search function supports more than 400 keywords. The IBIDS team is continually adding new keyword search terms to reflect emerging areas in dietary supplement research. For botanical entries, the IBIDS team uses the American Herbal Products Association's *Herbs of Commerce*, *2nd edition* as an authoritative source for Latin and other names of herbals and botanicals.

   The American Herbal Products Association and Michael McGuffin, who own the copyright to *Herbs of Commerce*, granted permission to embed *Herbs of Commerce* terms into the database and display them with search result sets. ODS also purchased botanical images photographed by Stephen Foster to use in the database and collected other images from copyright-free sources.

   IBIDS Health Outcomes**.** This feature presents article record sets of consumer interest on health outcomes of dietary supplements. IBIDS currently has five sets of information on health outcomes and dietary supplements, and each health outcome set contains a balanced overview of the outcome and its associated supplement. The IBIDS team updates the sets quarterly as part of the regular updates of the full IBIDS database.

   The current health outcomes available on the IBIDS site are:
   - Weight loss and calcium
   - Menopausal symptoms and botanicals
   - Athletic performance and creatine
   - Heart disease and omega-3 fatty acids
   - Falls and fractures in the elderly and vitamin D

   The IBIDS team monitors the use of health outcomes sets and plans to replace underused sets.

2. Promotion of IBIDS. Since 2004, ODS has promoted the IBIDS database at more than a dozen venues, including:

   - Medical Library Association's annual meeting
   - AARP national conference
   - American Public Health Association annual meeting
   - Society of Nutrition Education conference
   - American Dietetic Association's Food and Nutrition conference and expo
   - American Society of Pharmacognosists annual meeting
   - American Heart Association meeting
   - American College of Nutrition annual meeting
   - American Dietetic Association's Food and Nutrition conference and expo

3. IBIDS Clinical. IBIDS Clinical is a subset of IBIDS under development that is geared toward clinical practitioners and researchers. This project addresses an unmet need identified in a 2004 ODS review among clinicians for information on dietary supplements. During the initial planning phase, which began in mid-2005, ODS decided that IBIDS Clinical would have two major components, article records and organizational statements.

   The article records component draws from the full IBIDS database but, to be most relevant to clinicians, contains only records pertaining to the use of dietary supplements in humans. The IBIDS team classifies appropriate records based on the supplement(s) being tested and the evidence level and study design. Thus, the team organizes all records according to the following evidence pyramid, in which meta-analyses are at the top of the pyramid but are uncommon.:
   - Meta-analyses
   - Systematic reviews
   - Randomized controlled clinical trials
   - Other clinical trials
   - Observational studies
   - Case reports

   This structure allows users to review the evolution of the research base for a given dietary supplement or select records from studies with a given design. The IBIDS team based the definitions of the levels on information from the National Library of Medicine and the Agency for Healthcare Research and Quality's National Guideline Clearinghouse (www.guideline.gov).

   The pilot version of IBIDS Clinical included three dietary supplements: chromium, ginkgo, and vitamin E. By mid-2008, ODS had developed records on eight additional supplements: alpha-lipoic acid, black cohosh, creatine, magnesium, milk thistle, saw palmetto, St. John's wort, and vitamin D.

Appendix L: Computer Access to Research on Dietary Supplements (CARDS)

1. The Office of Dietary Supplements (ODS) periodically updates the CARDS database with information on dietary supplement-related projects funded by the Institutes and Centers (ICs) of the National Institutes of Health (NIH) and other Federal agencies for each fiscal year. The table below provides information on the updates to CARDS since its launch in 1999.

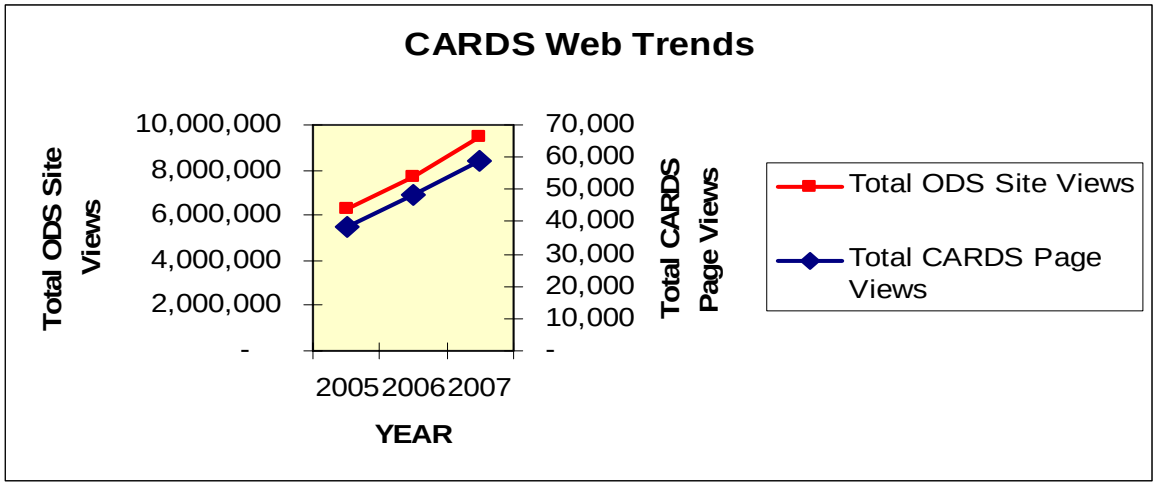
Records added to CARDS for Fiscal Years 1999–2006			
Project Funder and Fiscal Year of Funding	**Date Updated**	**Number of Records Added**	**Total Number of Records**
NIH, FY2006 U.S. Department of Agriculture (USDA), FY2005	1/2008	1,322	7,509
USDA, FY2004	8/2007	264	6,187
NIH, FY2005 USDA, FY2003	12/2006	1,338	5,923
USDA, FY2001–FY2002 Department of Defense, FY1999–FY2004*	4/2006	538	4,585
NIH, FY2004	1/2006	963	4,047
NIH, FY2003	4/2005	860	3,084
USDA, FY1999–2000	1/2005	475	2,224
NIH, FY2002	12/2003	569	1,749
NIH, FY2001	3/2003	443	1,180
NIH, FY2000	12/2002	363	737
NIH, FY1999	Launch in 1999	374	374

*ODS added seven additional records for NIH grants funded in FY2000–FY2002 during this update to complete the dataset for these years.

2. Recent publications by ODS CARDS Program staff:

Haggans CJ, Regan KS, Brown LM, Wang C, Krebs-Smith J, Coates PM, et al. Computer access to research on dietary supplements: a database of federally funded dietary supplement research. J Nutr. 2005 Jul;135(7):1796-9.

3. CARDS Web trends: Increases in “hits” on ODS and CARDS Web sites.



Appendix M: Federal Dietary Supplement Working Group

Member as of March 2008

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Stephen A. Wise, Ph.D., Chief, Analytical Chemistry Division, Chemical Science Laboratory, National Institute of Standards and Technology

Lawrence N. Yager, Ph.D., Scientific Initiatives Manager, Division of Research Infrastructure, National Center for Research Resources, NIH

Andrew J. Young, Ph.D., Chief, Military Nutrition Division, U.S. Army Research Institute of Environmental Medicine

Appendix N: Vitamin D Initiative

1. The evidence-based report from the Agency for Healthcare Quality and Research, *Effectiveness and Safety of Vitamin D in Relation to Bone Health,* is available at: http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat1b.chapter.73328

2. The proceedings of the conference, Vitamin D and Health in the 21st Century: An Update, which took place on September 5-6, 2007, are available on the Office of Dietary Supplements (ODS) Web site, at http://ods.od.nih.gov/News/AJCN2008.aspx. A description of the workshop is available at http://vitamindandhealth.od.nih.gov/.

3. The agenda for the late-breaking symposium, Vitamin D and Health in the 21st Century: Research Needs and Tools for Researchers, by ODS at the 2008 Experimental Biology Annual Meeting on April 8, 2008 is available at http://ods.od.nih.gov/News/VitaminDandHealth_RNTR.aspx.

4. Recent publications from ODS vitamin D initiative staff:

   Brannon PM, Yetley EA, Bailey RL, Picciano MF. Summary of roundtable discussion on vitamin D research needs. Am J Clin Nutr. 2008 Aug;88(2):587S-92S.

   Brannon PM, Yetley EA, Bailey RL, Picciano MF. Overview of the conference "Vitamin D and Health in the 21st Century: an Update." Am J Clin Nutr. 2008 Aug;88(2):483S-90S.

   Davis CD, Dwyer JT. The "sunshine vitamin": benefits beyond bone? J Natl Cancer Inst. 2007 Nov 7;99(21):1563-5.

   Davis CD, Hartmuller V, Freedman DM, Hartge P, Picciano MF, Swanson CA, et al. Vitamin D and cancer: current dilemmas and future needs. Nutr Rev. 2007 Aug;65(8 Pt 2):S71-4.

   Raiten DJ, Picciano MF. Vitamin D and health in the 21st century: bone and beyond. Executive summary. Am J Clin Nutr. 2004 Dec;80(6 Suppl):1673S-7S.

   Yetley EA. Assessing the vitamin D status of the US population. Am J Clin Nutr. 2008 Aug;88(2):558S-64S.

Appendix O: Use of Dietary Supplements by the Military

1. ODS staff wrote the following publications and made the following presentations on the use of dietary supplements by military personnel:

   Coates PM. Dietary supplements and health: the research agenda. Novartis Found Symp. 2007;282:202-7; discussion 207-18.

   Costello RB. Fostering research on dietary supplements to improve optimal physical and mental performance. Paper presented at the 76th Annual Aerospace Medical Association meeting, March 2005, St. Louis, MO.

   Costello RB. Guiding a research agenda on performance enhancing dietary supplements. Paper presented at the 75th Annual Aerospace Medical Association Meeting, May 2004, Anchorage, AK.

   Costello RB, Chrousos GP. Other bioactive food components and dietary supplements. In: Committee on Military Nutrition Research, Food and Nutrition Board, Institute of Medicine, editor. Nutrient composition of rations for short-term, high-intensity combat operations. Washington, DC: National Academies Press, 2005.

   Fomous CM, Costello RB, Coates PM. Symposium: conference on the science and policy of performance-enhancing products. Med Sci Sports Exerc. 2002;34:1685-90.

   Marriott BM, Kanter M. The role of dietary supplements for physically active people. Am J Clin Nutr. 2000;72(2 Suppl):504S-6S.

2. The Institute of Medicine released the following report:

   Greenwood MRC, Oria M, editors. Use of dietary supplements by military personnel, Committee on Dietary Supplement Use by Military Personnel, Food and Nutrition Board. Washington, DC: The National Academies Press, 2008.

Appendix P: Nutrient Intake Reference Values

1. Recent publications from Office of Dietary Supplement Nutrient Intake Reference Values Program staff:

Ashwell M, Lambert JP, Alles MS, Branca F, Bucchini L, Brzozowska A, et al. How we will produce the evidence-based EURRECA toolkit to support nutrition and food policy. Eur J Nutr. 2008 Apr;47 Suppl 1:2-16.

Baird S, Dwyer J, Evans E. Overview of nutritional assessment. Coleman LA, editor. Nutrition and rheumatic disease. Totowa, NJ: Humana Press, 2008:15-38.

Balk EM, Horsley TA, Newberry SJ, Lichtenstein AH, Yetley EA, Schachter HM, et al. A collaborative effort to apply the evidence-based review process to the field of nutrition: challenges, benefits, and lessons learned. Am J Clin Nutr. 2007;85:1448-56.

Chao SY, Houser RF, Tennstedt S, Jacques P, Dwyer JT. Food and nutrition care indicators: experts' views on quality indicators for food and nutrition services in assisted-living facilities for older adults. J Am Diet Assoc. 2007 Sep;107(9):1590-8.

Chumlea WC, Cockram DB, Dwyer JT, Han H, Kelly MP. Nutritional assessment in chronic kidney disease. In: Byham-Gray LD, Burrowes JD, Chertow GM, editors. Nutrition in kidney disease. Totowa, NJ: Humana Press, 2008:49-122.

Dwyer J, Stuart MA, Hendricks KM. Community nutrition and its impact on children: industrialized countries. In: Duggan C, Watkins JB, Walker WA, editors. Nutrition in pediatrics, 4th edition. Hamilton, Ontario: BC Decker, 2008:153-166.

Dwyer JT. Do functional components in foods have a role in helping to solve current health issues? J Nutr. 2007 Nov;137(11 Suppl):2489S-92S.

Erdman JW Jr, Balentine D, Arab L, Beecher G, Dwyer JT, Folts J, et al. Flavonoids and heart health: proceedings of the ILSI North America Flavonoids Workshop, May 31-June 1, 2005, Washington, DC. J Nutr. 2007 Mar;137(3 Suppl 1):718S-37S.

Fogli-Cawley JJ, Dwyer JT, Saltzman E, McCullough ML, Troy LM, et al. The 2005 Dietary Guidelines for Americans and risk of the metabolic syndrome. Am J Clin Nutr. 2007 Oct;86(4):1193-201.

Fogli-Cawley JJ, Dwyer JT, Saltzman E, McCullough ML, Troy LM, Meigs JB, et al. The 2005 Dietary Guidelines for Americans and insulin resistance in the Framingham Offspring Cohort. Diabetes Care. 2007 Apr;30(4):817-22.

Fogli-Cawley JJ, Dwyer JT, Saltzman E, McCullough ML, Troy LM, Jacques PF. The 2005 Dietary Guidelines for Americans Adherence Index: development and application. J Nutr. 2006 Nov;136(11):2908-15.

Marcotte L, Hennessy E, Dwyer J, Hyatt RR, Goldberg JP, Naumova EN, et al. Validity and reliability of a calcium checklist in early elementary-school children. Public Health Nutr. 2008 Jan;11(1):57-64.

Pfeiffer CM, Johnson CL, Jain RB, Yetley EA, Picciano MF, Rader JI, et al. Trends in blood folate and vitamin B-12 concentrations in the United States, 1988-2004. Am J Clin Nutr. 2007;86:718-27.

Pfeiffer CM, Osterloh JD, Kennedy-Stephenson J, Picciano MF, Yetley EA, Rader JI, et al. Trends in circulating concentrations of total homocysteine among US adolescents and adults: findings from the 1991-1994 and 1999-2004 National Health and Nutrition Examination Surveys. Clin Chem. 2008;54:801-13.

Picciano MF, Dwyer JT, Radimer KL, Wilson DH, Fisher KD, Thomas PR, et al. Dietary supplement use among infants, children, and adolescents in the United States, 1999-2002. Arch Pediatr Adolesc Med. 2007;161:978-85.

Potischman N, Cohen BE, Picciano MF. Dietary recommendations and identified research needs for The National Children's Study. J Nutr. 2006 Mar;136(3):686-9.

Reaves L, Steffen LM, Dwyer JT, Webber LS, Lytle LA, Feldman HA, et al. Vitamin supplement intake is related to dietary intake and physical activity: The Child and Adolescent Trial for Cardiovascular Health (CATCH). J Am Diet Assoc. 2006 Dec;106(12):2018-23.

Yetley EA. Multivitamin and multimineral dietary supplements: definitions, characterization, bioavailability, and drug interactions. Am J Clin Nutr.2007;85:269S-76S.

Yetley EA. Science in the regulatory setting: a challenging but incompatible mix? Novartis Found Symp. 2007;282:59-68.

Yetley EA, Rader JI. Modeling the level of fortification and post-fortification assessments: U.S. experience. Nutr Rev. 2004;62:S50-9.