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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Part 2: A Review of ODS and Its Activities
(23 pages)

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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.

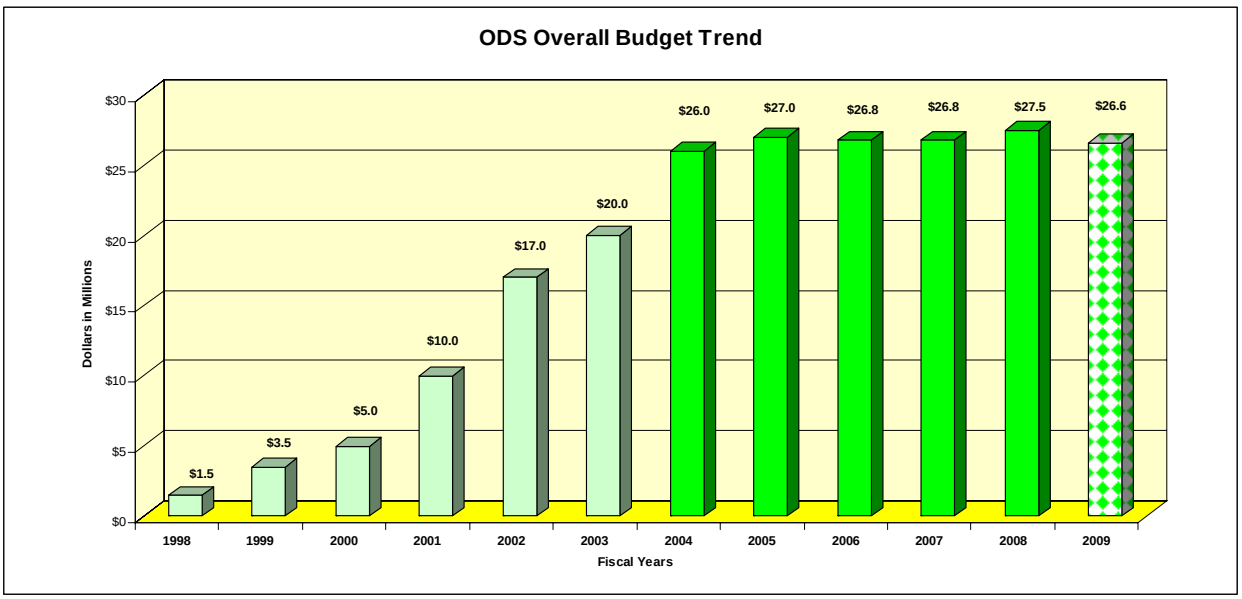
4. Promote and support the development and improvement of methodologies appropriate to the scientific study of dietary supplement ingredients.

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.

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.