



Draft Strategic Plan 2016–2021

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

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National Institutes of Health
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Draft Strategic Plan: 2016-2021

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FROM THE ODS DIRECTOR

As the lead federal entity for the scientific exploration of dietary supplements, the Office of Dietary Supplements (ODS) has achieved remarkable progress in advancing research and—equally importantly—translating the results of that research into valuable information for use by scientists, policymakers, health professionals, industry, and consumers. This progress has been possible only through the continued and evolving collaborations that ODS has forged with partners in the federal sector, including the National Institutes of Health (NIH) Institutes and Centers (ICs) and other federal agencies, as well as in the private and academic sectors.

About half the U.S. population uses dietary supplements on a regular basis. The array of products on the market is large, with ingredients that range from vitamins and minerals to herbs and other complex mixtures. The sale and availability of dietary supplements are governed by a law enacted in 1994 that allow them to be marketed based on the assumption that they are safe. In other words, regulations for foods, not drugs, apply to dietary supplements.

Consumers and health professionals have many questions about dietary supplements and their effects on health. To answer these questions, ODS takes a critical look at the science behind supplements, identifying gaps in knowledge that must be addressed and filling those gaps with the necessary research. ODS also develops and disseminates research tools to advance the science and works to increase the number of talented investigators who study dietary supplements, providing much-needed information to the public and informing public-health policy. The focus of dietary supplement research at ODS is on the efficacy, safety, and quality of these products. A variety of strategies are needed to address each of these factors, as this document conveys.

Since its inception in 1995, ODS has provided the vision and leadership needed to galvanize and support collaborations within and beyond NIH. These collaborations are integral to all of ODS's work. They capitalize on the talents and capabilities of ODS staff and other agencies and meet mutually beneficial goals. These collaborations are also efficient and cost effective because ODS does not duplicate the work of other agencies. ODS engages in international collaborative work as well—for example, with Health Canada to develop Dietary Reference Intake recommendations for nutrients and with agencies in many countries in the Vitamin D Standardization Program (described in section II).

The ODS staff are exceptionally talented, with national and international reputations for their work in such fields as analytical chemistry, pharmacognosy, biochemistry, epidemiology, clinical nutrition, dietetics, and health communications. Importantly, staff members have a shared vision and a collaborative spirit that enhances their roles in addressing complex and sometimes challenging issues.

ODS enters this 2016–2021 strategic planning period with a wealth of experience to guide it and a robust history of results that make a difference in people's lives. The office has developed tools

and resources that can help NIH and others advance its scientific investigations of dietary supplements. ODS's investigations are highly consistent with current NIH efforts to enhance transparency, rigor, and reproducibility in the conduct of science in general.

As ODS moves forward with future endeavors, the question that guides us will be: "What are the key emerging public health priorities that should drive our work?"

I. Background

The history of the Office of Dietary Supplements (ODS) is rooted in legislation—the Dietary Supplement Health and Education Act of 1994 (summarized below)—and subsequent congressional language that form the basis of its mission, vision, and programs. The National Institutes of Health (NIH) created ODS in 1995 and placed it in the Office of Disease Prevention (ODP) in the Office of the Director (OD) at NIH. ODS and ODP are now administratively located in the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) in the OD.

ODS Mandates in the Dietary Supplement Health and Education Act (DSHEA) of 1994 and Subsequent Congressional Language

ODS purpose:

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

ODS responsibilities:

- 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
- Collect and compile the results of scientific research relating to dietary supplements, including scientific data from foreign sources
- 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 connection 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

Congressional mandates to ODS subsequent to DSHEA:

- Develop a botanical research center initiative (1999)
- Conduct evidence-based reviews of the efficacy and safety of dietary supplements (2001)
- Accelerate the validation of analytical methods and reference materials for dietary supplements (2001)
- Support the development of a dietary supplement label database (2004)

Definition of a dietary supplement (from DSHEA):

- A product (other than tobacco) that is intended to supplement the diet and 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 humans to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combination of these ingredients
- Intended for ingestion in pill, capsule, tablet, or liquid form
- Not represented for use as a conventional food or as the sole item of a meal or diet

The ODS budget increased five-fold from \$1 million in 1996 to \$5 million in 2000, and then from \$5 million to \$25 million between 2000 and 2004. The budget remained relatively stable until 2015, when it declined by 8%. The ODS FY 2016 budget is \$25.3 million.

Through its activities, and consistent with the overall mission of DPCPSI, ODS helps NIH Institutes and Centers (ICs) strengthen existing programs in research and training and enhances the array of resources available to investigators and other ODS stakeholders.

This strategic plan capitalizes on ODS advances in past years to enhance tools for successful research, to build on remarkable collaborations with other ICs and federal agencies, and to forge public-private partnerships. The ultimate goals of these activities are to continue to build the scientific underpinnings for dietary supplement research and to provide resources that will better inform people about nutrition in general and dietary supplements in particular.

*The **mission** of ODS is to conduct and support scientific research and provide intellectual leadership for the purpose of strengthening the knowledge and understanding of dietary supplements to foster an enhanced quality of life and health for the U.S. population.*

*The **vision** of ODS is that researchers, health professionals, government officials, other policy makers, and consumers will have ready access to scientific information of the highest quality on the health effects of dietary supplements.*

II. ODS Accomplishments (2010–2015)

At over 20 years of age, the Office of Dietary Supplements (ODS) maintains its commitment to promoting the best science that can inform public health policy and consumers' decisions about their own health care. ODS uses its strategic planning cycles to submit itself to public scrutiny, describe the outcomes of its investments, and offer an opportunity for the public to provide input into its plans.

Every 5 years, ODS develops a new strategic plan based on a review of its recent accomplishments and challenges. The following goals were the focus of the ODS strategic plan for 2010–2014.

- **Goal 1:** *Provide intellectual leadership by fostering research to analyze and evaluate the role of dietary supplements in promoting health and reducing the risk of disease*
- **Goal 2:** *Expand the scientific knowledge base on dietary supplements by funding new research and training*
- **Goal 3:** *Support the development of research tools for the study of dietary supplements*
- **Goal 4:** *Make the most up-to-date scientific knowledge about dietary supplements publicly available*

ODS categorizes its programs and activities into five broad areas. Each area supports one or more of the ODS 2010–2014 goals:

1. Research and training (Goals 1 and 2)
2. Population studies and nutrient interventions (Goal 1)
3. Research resources (Goal 3)
4. Collaborations with other federal agencies (Goal 1, 2, and 3)
5. Translating research findings (Goal 4)

An ODS staff member oversees each program, and most ODS staff members are active in more than one program. Each program interacts with one or more stakeholder communities.

ODS activities in 2010–2014 within each of its five programmatic areas are summarized below. More details on these activities are available in the *Strategic Plan 2010–2014 Progress Report* published on the ODS website (https://ods.od.nih.gov/About/Strategic_Plan_2010-2014_Progress_Report.aspx). ODS invited comments on the report from the public, and it used the comments it received to shape the current strategic plan presented in Section III of this document.

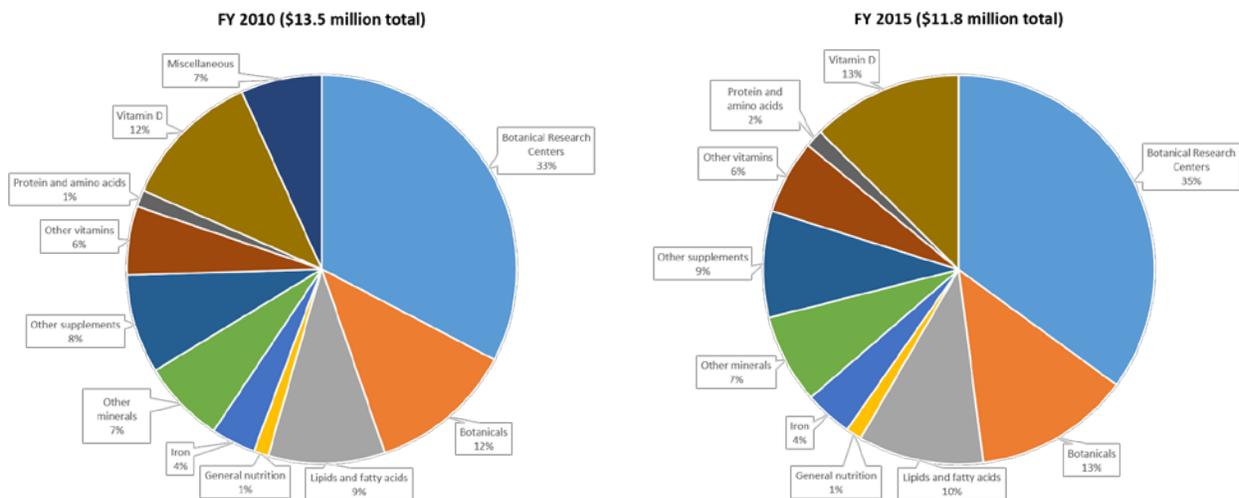
Area 1: Research and Training

Dietary Supplement Research. ODS supports research largely through grants that it co-funds with National Institutes of Health (NIH) Institutes and Centers (ICs) as well as through contracts and interagency agreements. From FY 2010 to FY 2014, ODS provided co-funding for 468 grants at a total investment of \$67.3 million. ODS funded research on dietary supplements has characterized

the use of these products by the public, described their composition in more detail, determined their effects on body functions, and has led to the development of new analytical technologies, all of which will enhance the quality of future dietary supplement research. Research planning activities—such as workshops, conferences, and symposia—provide critical input on new directions for the ODS research portfolio, give researchers access to ODS staff expertise on dietary supplement matters, and help ensure that the studies that ODS funds use well-characterized and high-quality products.

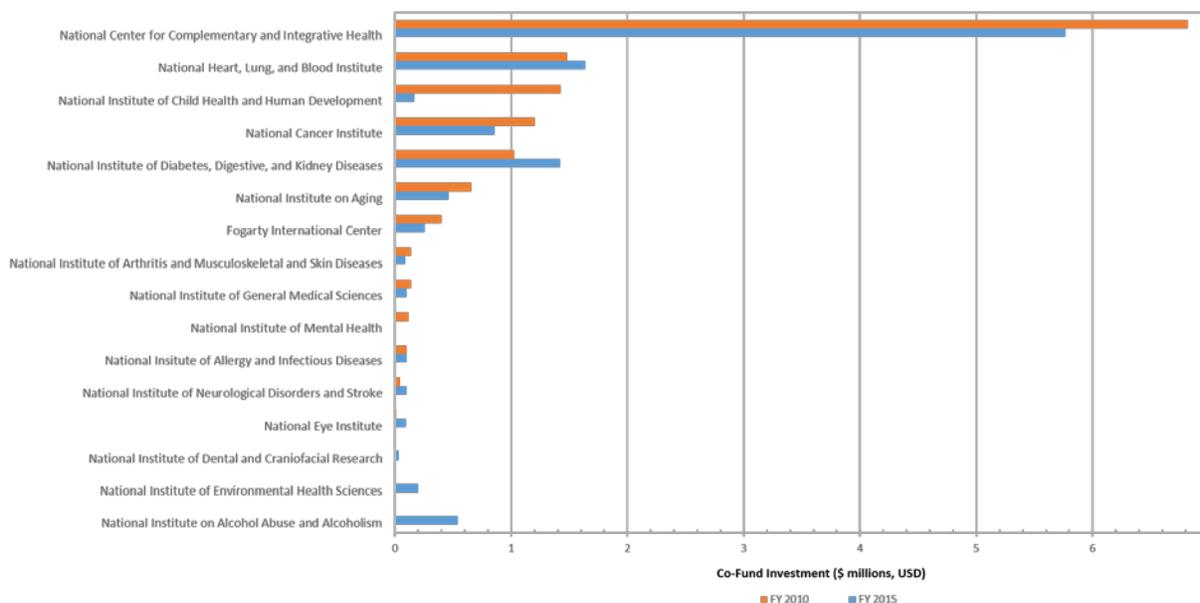
In FY 2010, ODS used 62% of its \$21.75 million budget to fund extramural research. In FY 2015, ODS spent a slightly smaller proportion of its \$20.21 million budget (58%) to support extramural investments in research. The research portfolios (by investment category) that ODS supported in FY 2010 and FY 2015 are shown in Figure 1. Of particular note is the increased spending on vitamin D and botanicals which reflect a response to public health priorities and emerging research opportunities.

**FIGURE 1:
FY 2010 and FY 2015 ODS EXTRAMURAL RESEARCH PORTFOLIOS,
BY INVESTMENT CATEGORY**



ODS co-funded grants with many NIH ICs from 2010 to 2015 (Figure 2). These partnerships are the key means by which ODS supports dietary supplement research.

**FIGURE 2:
NUMBER OF GRANTS CO-FUNDED BY ODS,
BY COLLABORATING NIH INSTITUTE/CENTER, FY 2010 AND FY 2015**



Botanical Research Centers (BRCs). ODS and its IC partners established several botanical research centers (BRCs) in response to a congressional mandate to ODS in 1999. In 2010, ODS, the National Center for Complementary and Alternative Medicine (now the National Center for Complementary and Integrative Health) and the National Cancer Institute issued 5-year awards for BRCs at Louisiana State University, University of Illinois at Chicago, University of Illinois at Urbana-Champaign, University of Missouri, and Wake Forest University. These BRCs studied the safety and mechanisms of action of botanicals in women’s health, metabolic syndrome, cancer, cardiovascular disease, and immune function. Between 2010 and 2015, investigators at these BRCs published 272 research articles in peer-reviewed journals. In 2015, ODS expanded the scope of the BRC program and changed its name to the NIH Centers for Advancing Research on Botanical and Other Natural Products (CARBON).

Training and Career Development. ODS has provided support for traditional NIH extramural mechanisms that offer training and career development opportunities to junior and mid-career scientists. In addition, ODS created the Intramural Research Scholars Program to provide opportunities for junior scientists in intramural NIH laboratories to conduct research on dietary supplements for 1 year.

Dietary Supplement Research Practicum. The Mary Frances Picciano Dietary Supplement Research Practicum is a multiday course on the NIH campus that provides dietary supplement and nutrition research training and career development opportunities to researchers, academic faculty members, students, and health professionals. Since 2007, this annual practicum has included presentations and discussions on issues, concepts, knowledge gaps, and controversies pertaining to dietary supplements and their ingredients. The practicum faculty consists of experts from ODS and other NIH ICs, academic institutions, federal regulatory agencies (such as the Food and Drug Administration [FDA] and the Federal Trade Commission [FTC]), industry, consumer watch-dog groups, media, and standard-setting organizations. Eligibility for the practicum was originally limited to full-time academic faculty members, doctoral students, postdoctoral researchers, and fellows in health-related disciplines as well as selected government employees and contractors. In 2012, ODS expanded eligibility to all health professionals and scientists with a postgraduate degree whose work involves dietary supplements; master's degree students; and medical, dental, and nursing students.

Area 2: Population Studies and Nutrient Interventions

Vitamin D Initiative. To advance scientific understanding of the importance of vitamin D to human health, ODS leads and collaborates in such activities as:

- An update [1] of an evidence-based review of the health effects of vitamin D and clinical vitamin D metabolites with the Agency for Healthcare Research and Quality (AHRQ) [2]
- The measurement of vitamin D exposure and status in the U.S. population with the Centers for Disease Control and Prevention (CDC) [3-6]
- The development of methods, standardized measures, and reference materials for vitamin D with the National Institute of Standards and Technology (NIST) [7]

ODS also co-funds grants for basic, epidemiological, and clinical research on vitamin D with NIH ICs. Finally, ODS established the international Vitamin D Standardization Program (VDSP) with the CDC and NIST to standardize the laboratory measurement of vitamin D status in national health surveys worldwide (see Program Profile I below) [8].

Folate and Vitamin B12 Monitoring in the United States. ODS scientists have collaborated with experts at the CDC to review and analyze National Health and Nutrition Examination Survey (NHANES) data on folate and vitamin B12 intake and status. ODS scientists have published these analyses in peer-reviewed journals and presented their findings at national and international meetings [9-14]. In 2010, ODS convened a roundtable of experts and scientists to discuss the measurement of folate and vitamin B12 status biomarkers in NHANES and to identify research gaps. ODS and colleagues who participated in the roundtable published nine articles on the meeting proceedings in a supplement to the *American Journal of Clinical Nutrition* [15]. To improve the accuracy of the laboratory measurement of homocysteine and folate in serum, ODS and NIST jointly developed a Standard Reference Material (SRM) for measuring the levels of these metabolites in frozen human serum.

Program Profile I: Vitamin D Initiative

ODS has taken a lead role in the federal government to advance scientific understanding of the role of vitamin D in health. In 2011, the Institute of Medicine (now the National Academy of Medicine) released a report on the dietary reference intakes (DRIs) for vitamin D and calcium, highlighting issues such as the need for studies demonstrating dose-response relationships, more systematic measurement of health outcomes, and reliable and standardized indicators of exposure (including 25-hydroxyvitamin D [25(OH)D], the most commonly used marker of vitamin D status). ODS has used the research agenda from the Institute of Medicine report (to which it contributed both intellectually and financially) to plan its ongoing activities related to vitamin D.

In 2013, ODS worked with the Agency for Healthcare Research and Quality (AHRQ) to update a 2009 systematic review on vitamin D research with evidence from more recent studies related to health outcomes of vitamin D alone or in combination with calcium. The authors of the update, issued in September 2014 [1], concluded that despite the availability of additional research since publication of the initial report, data remained inconclusive on the health benefits of vitamin D other than those related to bone. This update informed an ODS-sponsored conference, "Vitamin D: Moving Toward Evidence-Based Decision Making in Primary Care." The conference, held in December 2014, began with an acknowledgement that data were still lacking on other health benefits and addressed the evaluation and application of evidence for decision making by primary care practitioners, approaches for counseling about vitamin D in primary care settings when data are uncertain, and issues surrounding laboratory measurement of serum 25(OH)D. The workshop also addressed the 2014 U.S. Preventive Services Task Force report that concluded that evidence was insufficient to evaluate the benefits and harms of screening adults who have no symptoms for vitamin D deficiency.

In 2013, ODS initiated a collaboration with the Nutrient Data Laboratory at the U.S. Department of Agriculture (USDA) to examine exposure to vitamin D. Although both sunlight and supplements can serve as sources of vitamin D, estimates of total vitamin D exposure must also take dietary vitamin D intakes into account. Notably, current estimates of the amounts of vitamin D in foods do not include the 25(OH)D content of animal-based foods, which can lead to underestimates of total vitamin D exposure. The USDA collaboration explored both analytical approaches to measuring 25(OH)D in foods and the effect of including the 25(OH)D content of foods on total estimates of vitamin D exposure.

In 2010, ODS established the international Vitamin D Standardization Program (VDSP) in conjunction with the Centers for Disease Control and Prevention (CDC) and the National Institute of Standards and Technology (NIST). In addition, an ODS collaboration with NIST led to the development of a reference measurement system for vitamin D that includes a reference measurement procedure and clinical vitamin D metabolite Standard Reference Materials. Academic researchers and healthcare laboratories use these tools to make sure that clinical metabolite analyses yield consistent and accurate results. ODS also supported the development of a study design for standardizing past vitamin D measurements.

ODS, in collaboration with CDC and NIST, designed and conducted studies that compare the vitamin D measurement results of different laboratories. With ODS support, CDC established a program in 2012 to certify laboratories that measure vitamin D levels in blood that will complement ongoing VDSP efforts. Through this program, efforts are underway to ensure that manufacturers' assays for measuring vitamin D levels in blood yield the same results as the NIST reference measurement procedure. In addition, the ODS-sponsored NIST-NIH Vitamin D Metabolites Quality Assurance Program and Vitamin D External Quality Assurance Scheme help clinical and research laboratories use commercial clinical vitamin D kits properly. In 2013, VDSP began comparing the results from the national health and nutrition surveys of countries participating in the VDSP for vitamin D levels in blood and reported vitamin D intakes. This program will complement ongoing VDSP efforts.

Evaluation of Dietary Supplement Use in the United States and Relationship to Health and Disease Risk. ODS collaborates with NIH researchers (e.g., from the National Cancer Institute and the Office of Disease Prevention), other government agencies (e.g., CDC and U.S. Department of Agriculture [USDA]), academia, and private consulting companies to evaluate dietary supplement

use in the United States. ODS and partner scientists analyze data on use of all supplements and of individual nutrients (e.g., iodine, calcium, and vitamin D) and reasons for use in adults and children. We have reported the results in peer-reviewed journals and workshop presentations [5, 13, 16-38]. In addition, ODS investigators have compared the contribution of nutrient intake from dietary supplements with the total intake of nutrients from all sources.

Nutrition and Dietary Supplement Interventions for Inborn Errors of Metabolism (IEM) and Primary Mitochondrial Diseases. ODS established this initiative in 2010 in collaboration with the NIH Office of Rare Diseases Research to identify gaps in research on the safety, efficacy, and effectiveness of nutritional management strategies, including dietary supplements, for IEM.

In January 2011, NIH convened a meeting of federal partners to engage the metabolic disease research community and develop a plan to promote evidence-based research on nutrition and dietary supplement interventions used in IEM. ODS sponsored a workshop in December 2011 to address challenges and share successes in IEM research. One outcome of these efforts has been the development of a research agenda to guide the metabolic disease community in the conduct of research on the safety and efficacy of nutritional interventions and dietary supplement use in IEM [39].

In collaboration with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the Office of Rare Diseases Research at NIH, ODS held a workshop in December 2014 on nutritional interventions (including dietary supplements) in primary mitochondrial diseases. The workshop goals were to identify gaps in knowledge, develop a research agenda, and identify research opportunities that will promote an evidence base for use of these therapies in primary mitochondrial diseases. The executive summary of the meeting workshop is available on the ODS website (https://ods.od.nih.gov/News/Mito2014_ExecutiveSummary.aspx).

Currently, the IEM initiative is developing research approaches that are suitable for the study of all rare disorders and is evaluating the safety and efficacy of dietary interventions for IEM. These activities fit into the broader context of public health because they will likely lead to better approaches to manage diseases that affect millions of people.

Area 3: Research Resources

Analytical Methods and Reference Materials (AMRM) Program. Researchers use analytical methods for the quantitative and qualitative analysis of both dietary supplement raw materials and finished products. Ideally, these materials generate reliable, accurate data for use by manufacturers, regulators, and researchers when characterizing these materials and products. Similarly, certified reference materials (CRMs) and SRMs are necessary for the development, use, calibration, and evaluation of the methods. Validated analytical methods and CRMs allow analysts to demonstrate that measurements are accurate, precise, and reproducible. The results of these analyses enhance consumer confidence in the quality of marketed dietary supplements and ensure

confidence in the results of research on dietary supplements. The major components of the AMRM program are methods development, methods validation, reference material development, education and outreach, and laboratory performance evaluation. This program is more fully described in Program Profile II below.

Program Profile II: Analytical Methods and Reference Materials Program (AMRM)

The goals of the AMRM program are to:

1. Develop and expand the availability and use of validated, reliable, and accurate analytical techniques for quantitative and qualitative characterization of dietary supplements and their ingredients
2. Produce and make available reference materials appropriate for analytical method development, validation, and demonstration of laboratory proficiency as well as for basic, preclinical, and clinical studies on the biological effects of dietary supplements in health and disease
3. Support public-private partnerships that will increase emphasis on chemical and biological characterization of dietary supplements and their bioactive ingredients as a scientifically sound approach to exploring and understanding their biological effects on health and disease
4. Disseminate information and data about validated analytical methods and reference materials in the peer-reviewed scientific literature and publicly to expand their use by the informed ODS stakeholder community

Authentic dietary supplement ingredient reference materials with assigned values for concentrations of active and/or marker compounds, pesticides, and toxic metals assist in the verification of manufacturers' label claims and in quality control during the manufacturing process. Through an interagency agreement with the National Institute of Standards and Technology (NIST), AMRM supports the development of dietary supplement matrix (Standard Reference Materials (SRMs), (e.g., green tea, berries, and soy materials).

Participants in the Dietary Supplement Laboratory Quality Assurance Program, which ODS administers in partnership with NIST, measure concentrations of active and/or marker compounds and nutritional and toxic elements in practice and test materials. Participants receive reports on the accuracy of their results and how their findings compare to those of NIST and other laboratories. The program also holds workshops to discuss results and advances in methodologies for characterizing dietary supplements and to provide guidance on improving laboratory performance.

Accurate measurements of biomarkers are vital for estimating the public health impact of nutrients. AMRM supports an interagency agreement with NIST to create serum-based SRMs for nutrient biomarkers (e.g., vitamin D metabolites, vitamin B6 metabolites, and fatty acids) and to develop and implement laboratory quality assurance programs for nutrient biomarker measurements in clinical specimens.

With other National Institutes of Health Institutes and Centers, AMRM supports the validation of methods used in biomedical research on botanicals and other dietary supplement ingredients. For example, ODS and the National Center for Complementary and Integrative Health co-funded administrative supplements to existing grants in 2010–2012 for validation studies of analytical methods for natural products. ODS also provided funding to the the U.S. Department of Agriculture's Food Composition and Methods Development Laboratory to support the development of chemical fingerprinting and other techniques to verify the identity of botanicals.

ODS has launched a new version of the AMRM program's website (<https://ods.od.nih.gov/Research/AMRMProgramWebsite.aspx>). The new site is easier for stakeholders to navigate and includes a searchable database of analytical methods.

Dietary Supplement Databases. ODS funded and led the development of two databases of information on the composition of many dietary supplements for sale in the United States. The Dietary Supplement Label Database (DSLDD) provides product information taken directly from supplement labels. An internet-based version of the DSLDD is available (<http://www.dsld.nlm.nih.gov/dsld/>), and ODS will release a mobile version for smartphones later in 2016.

A second database, the Dietary Supplement Ingredient Database (DSID; <http://dsid.usda.nih.gov>), provides analytically derived estimates of amounts of ingredients in a nationally representative sample of popular dietary supplements.

ODS also supports and is currently updating an internet-based database, Computer Access to Research on Dietary Supplements (CARDS). CARDS, available at https://ods.od.nih.gov/Research/CARDS_Database.aspx, contains information on research projects pertaining to dietary supplements.

These efforts are more fully described in recent publications [40-56] and in Program Profile III below.

Program Profile III: Dietary Supplement Databases

The Dietary Supplement Ingredient Database (**DSID**) contains analytically derived information on the amount of labeled ingredients of many dietary supplements offered for sale in the United States. The DSID currently includes adult, child and prenatal multi-vitamin/multimineral supplements and omega-3 fatty acid products. The Dietary Supplement Label Database (**DSLDD**) is a repository for all the information on the product label (composition, claims, manufacturer contact information, etc.) of dietary supplements. The database has data from about 60,000 labels, and the Office of Dietary Supplements (ODS) adds data from another 1,000 labels each month. Using these databases with food composition databases makes it possible to estimate the total daily intakes of nutrients and other bioactive substances from both foods and dietary supplements.

Since 2004, the Federal Dietary Supplement Database Working Group has advised ODS on developing, launching, and expanding the DSID, DSLDD, and CARDS (Computer Access to Research on Dietary Supplements). The working group consists of representatives from the National Institutes of Health (NIH) (ODS, National Library of Medicine, and National Cancer Institute), USDA (U.S. Department of Agriculture), the Centers for Disease Control and Prevention, the U.S. Food and Drug Administration, Department of Defense (DoD), and the National Institute of Standards and Technology. Since 2010, this working group has developed criteria for choosing botanicals and other dietary ingredients of public-health interest to add to the DSID that do not have established recommended intakes but that should be analytically evaluated. This prioritization process led to the decision to focus first on adding data on green tea products to the DSID, and a pilot study on these products has been completed.

Between 2010 and 2014, ODS and its collaborators published papers and gave presentations on using the DSID and/or DSLDD at more than 28 national meetings to health professionals, industry representatives, educators, and others.

Another ODS-supported database, CARDS, contains information on research projects pertaining to dietary supplements funded by the USDA, DoD, or NIH since 1999.

Systematic Reviews. ODS developed an evidence-based review program through ARHQ's Evidence-based Practice Center program. To date, this ODS program has sponsored 17 systematic reviews on topics related to dietary supplements, including B-vitamins, ephedra, multivitamin/mineral supplements, omega-3 fatty acids, soy, probiotics, and vitamin D. These reviews have informed the development of research agendas for ODS and its NIH partners. They have also informed the development of Dietary Reference Intakes (DRIs) for calcium and vitamin D as well as clinical practice related to these nutrients.

Area 4: Collaborations with Other Federal Agencies

Federal Working Group on Dietary Supplements. ODS established the Federal Working Group on Dietary Supplements. The working group's members represent most NIH ICs as well as several other federal agencies (AHRQ, Administration for Community Living, CDC, Consumer Product Safety Commission, DoD, Department of Justice, Department of Veterans Affairs, FDA, FTC, Health Resources and Services Administration, National Aeronautics and Space Administration, NIST, Office of Disease Prevention and Health Promotion, U.S. Agency for International Development, and USDA). This group has met twice a year since January 2005 to strengthen individual agency and collaborative efforts involving dietary supplement research, education, and communication.

Several descriptions and program profiles of ODS programs in this document mention additional ODS collaborations with federal agencies. The following collaborations are examples of ODS' ability to catalyze research partnerships and serve as an advisor to federal agencies on topics related to dietary supplements:

FDA. ODS provides expert consultation to FDA staff and has collaborated with them to create systematic reviews (e.g., of probiotic safety) and organize conferences. FDA and ODS are co-leads on the recently formed microbiome working group to coordinate related activities.

USDA. ODS collaborations with the USDA Agricultural Research Service include funding the DSID, developing and validating research methods to identify ingredients in botanicals, and establishing the John A. Milner Postdoctoral Fellowship Program.

DoD. ODS helps the DoD study the use, safety, and efficacy of dietary supplements in military populations. ODS also helps DoD educate warfighters about the benefits, risks, and proper use of such products. Finally, ODS provides expert consultation to DoD staff and ODS staff serve on DoD advisory committees.

Area 5: Translating Research Findings

Communications. ODS communication efforts include a broad spectrum of outreach activities, such as maintaining the ODS website, engaging with social media, responding to media and public inquiries, and developing useful information for consumers and health professionals. Two ODS newsletters (available at https://ods.od.nih.gov/News/ODS_Update.aspx) have wide readerships, and ODS disseminates each one electronically to over 7,000 addresses. ODS staff scientists

frequently give seminars at scientific and professional conferences, workshops, and lectures for university courses. See details in Program Profile IV.

Public Health Policy and Clinical Practice Related to Dietary Supplements. ODS has supported the development of Dietary Reference Intakes (known as DRIs in the United States and Canada) and research on the science underpinning these values and their application. Although the original intent of DRIs was to help ensure that adults and children have adequate nutrient intakes, ODS is now studying whether it is possible to establish such values for the use of dietary supplements to prevent chronic diseases.

Program Profile IV: Communicating the Science of Supplements

The Office of Dietary Supplements (ODS) gives priority to communicating the science of supplements to its diverse audiences by providing results of scientific research on dietary supplements. ODS also offers advice and tools on how to use this information to make informed decisions about personal health. The ODS Communications Program provides helpful, up-to-date information on dietary supplements through various channels, including social media platforms. The ODS website, its main means of communication and home to its informational resources, receives over 1.5 million visits per month. ODS communications staff respond directly to media inquiries and questions from the public about dietary supplements.

Fact sheets on dietary supplement ingredients are the most frequently viewed materials on the ODS website. More than two dozen fact sheets are available, primarily on nutrients such as vitamin D and magnesium. The website includes detailed versions with references directed to health care providers as well as easy-to-read versions for consumers in both English and Spanish. Fact sheets are also available on certain types of dietary supplements (such as multivitamin/mineral products) and on supplements marketed for specific purposes (such as weight loss). ODS is continually developing new fact sheets, revising current ones and linking to informational resources on dietary supplements from throughout the federal government from its website. ODS intends to become the primary source for anyone looking for information about these products.

The ODS website provides detailed descriptions of ODS program areas and activities, including the Analytical Methods and Reference Materials program (see Program Profile II), vitamin D initiatives (see Program Profile I), iodine, and iron.

Information on the ODS website that is particularly relevant to the scientific research community includes research-funding opportunities, a listing of grant applications that ODS has funded, databases of information on the composition of many dietary supplements in the marketplace (see Program Profile III), and the ability to limit searches of the biomedical literature in PubMed to citations from the dietary supplement literature. Through the ODS website, users can sign up to receive e-newsletters, such as *ODS Update* (directed to professional audiences) and *The Scoop* (for consumers), as well as email blasts on special topics. And every workday, ODS posts information about dietary supplements or nutrition on Twitter and Facebook.

III. The 2016–2021 Strategic Plan: Translating Office of Dietary Supplements Goals into Action

This 2016–2021 Office of Dietary Supplements (ODS) strategic plan captures the momentum of current ODS programs and activities and reflects the many evaluative comments received from various sources. ODS will continue to prioritize its efforts based on public health needs. Its experience in building capacity related to vitamin D in particular has taught ODS much about how to approach other emerging public health research opportunities. Building and expanding key partnerships with National Institutes of Health (NIH) Institutes and Centers (ICs) and offices and with other federal agencies will continue to be a focus for ODS. Through these partnerships, ODS contributes to funding research and workforce development; identifying areas of research need; and developing tools and resources for researchers, regulators, and industry.

In identifying research needs, developing resources, and establishing key partners and communication strategies, ODS takes a multipronged approach that is guided by several key questions:

- What is the nature of the public health issue? Is the intake of a nutrient or other supplement ingredient too low or too high? What is the evidence?
- How are nutritional status and bioavailable levels of dietary supplement metabolites measured? What are the concerns about the reliability of the measures?
- What is the evidence on the health effects of dietary supplements? What levels of dietary supplements influence the observed effects?
- How should ODS and the research community fill the gaps in knowledge?
- How should ODS and its partners translate the results of research for policy makers, clinicians, and the public?

Mission

The mission of ODS is to conduct and support scientific research and provide intellectual leadership for the purpose of strengthening the knowledge and understanding of dietary supplements to foster an enhanced quality of life and health for the U.S. population.

Vision

The vision of ODS is that researchers, health professionals, government officials, other policy makers, and consumers will have ready access to scientific information of the highest quality on the health effects of dietary supplements.

To strengthen the knowledge and understanding of dietary supplements, ODS programs in 2016–2021 will focus on achieving the four goals below:

Goal 1: Expand the knowledge base on dietary supplements by stimulating and supporting a full range of relevant research and by developing and contributing to collaborative initiatives, workshops, meetings and conferences.

Goal 2: Enhance the dietary supplement research workforce through training and career development.

Goal 3: Foster development and dissemination of research resources and tools to enhance the quality of dietary supplement research.

Goal 4: Translate dietary supplement research into useful information for consumers, health professionals, and policymakers.

ODS will measure the success of its activities to address these goals based the relevance of publications in the peer reviewed literature arising from co-funded grants, research tools developed, information pieces written, initiatives and workshops developed by staff, and manuscripts published by staff. ODS will assess the impact of these results over time as they inform policy and influence health practices related to dietary supplements.

GOAL 1: Expand the knowledge base on dietary supplements by stimulating and supporting a full range of biomedical research and by developing and contributing to relevant initiatives, workshops, meetings, and conferences.

Today, at least 75,000 dietary supplement products are available that contain vitamins and minerals, herbs and botanicals, and other ingredients (such as glucosamine, fish oils, and probiotics). Yet there are questions about the efficacy and safety of many dietary supplements. ODS plans to continue working in collaboration with NIH ICs and other research institutions to answer such questions. As it does now, ODS will choose research priorities based on their public health importance, and it will use systematic reviews as a primary assessment tool to address efficacy and safety issues. ODS will also use systematic reviews to translate research results for public health policy decision making.

Strategy 1-1: Increase understanding of the biological effects, health impacts, and use of dietary supplements.

ODS will support innovative research on the usage of dietary supplements, their health effects, and their underlying biological mechanisms. In addition to co-funding new research with partner NIH ICs, ODS will continue to expand its ability to promote research on dietary supplements by providing supplemental funding to existing NIH grants, thus stimulating more investigations of dietary supplements' health effects.

In a joint effort with the National Center for Complementary and Integrative Health (NCCIH), ODS will continue to support transdisciplinary research to characterize the active components and health effects of inherently complex botanical dietary supplements. The NIH Centers for Advancing Research on Botanical and Other Natural Products (CARBON) program will continue to conduct preclinical research to inform future clinical trials and the acceleration of state-of-the-art, high-throughput, and high-content method development.

ODS will support research on the identification and measurement of biological measures or biomarkers of nutrient exposure and status in relation to chronic disease in populations and individuals.

Recent research, such as that supported by the NIH Human Microbiome Project, has revealed many insights into the influence of human-associated microbes on health and nutrition and has raised many more questions. ODS will seek to further understand the role of the microbiome in mediating the effects of bioactive components of food and dietary supplements. ODS will remain committed to supporting novel research, workshops, symposia, and trans-federal agency efforts aimed at elucidating the functional relevance of the microbiota to nutritional status, energy balance, and risk of disease.

Strategy 1-2: Conduct research on patterns of dietary supplement use in the U.S. population.

ODS staff will assess the prevalence, frequency, duration, levels, and types of dietary supplements used in the United States. For example, ODS plans to use National Health and Nutrition Examination Survey data to investigate dietary supplement usage patterns in specific population cohorts (such as seniors, Native American communities, pregnant women, or cancer survivors) and consumer use of dietary supplements in combination with widely used over-the-counter and prescription medications. ODS also plans to evaluate the cognitive and behavioral factors underlying dietary supplement use.

ODS will address methodological issues related to assessment of supplement usage in epidemiologic and other study designs. It will also evaluate current and novel laboratory methods to measure supplement usage and nutritional status for individual ingredients in supplements.

Strategy 1-3: Identify knowledge gaps and research needs.

ODS will support and co-sponsor systematic reviews of dietary supplements and their ingredients. Topics will include the efficacy and safety of supplement use and their potential role in reducing disease risk. ODS will also sponsor systematic reviews to assess the strength and quality of the science on the health effects of dietary supplements and their ingredients.

ODS will continue to conduct internal and NIH-wide portfolio analyses with NIH ICs and other federal partners, leading to priority setting for funding decisions and identification of emerging research opportunities.

ODS will lead and sponsor workshops and conferences with NIH ICs and offices to discuss and evaluate the current state of the science. These activities will include dietary supplement researchers, clinicians, government officials, industry representatives, and other stakeholders.

GOAL 2: Enhance the dietary supplement research workforce through training and career development.

Despite the widespread use of dietary supplements, the scientific investigation of many of these products and their ingredients remains a relatively new and small field. Therefore, funding is needed to develop and support a cadre of researchers who study dietary supplements and view their work as a recognized, important, and productive area of investigation.

Strategy 2-1: Support scientific training programs and continuing education activities.

The cofunding that ODS provides to extramural researchers will also give access to ODS staff expertise. ODS will continue to co-fund training grants and career development grants with partner ICs to train junior scientists in methodologies that will enhance dietary supplement research. All components of the CARBON centers, for example, will train young investigators (students, postdoctoral fellows, and new faculty) and encourage recruitment of junior researchers through the support of innovative pilot projects.

ODS will continue its new program that provides administrative supplements to awarded grants for up to a year. This will allow investigators, including junior scientists, to expand the scientific scope of their NIH-funded projects to include work related to dietary supplements.

The ODS will expand the Mary Frances Picciano Dietary Supplement Research Practicum by identifying ways to increase attendance, possibly with a live webcast of future practicums. ODS will also consider broadening the practicum's reach through a video archive of the most recent practicum and/or a repository of presentations from selected practicum speakers.

Strategy 2-2: Provide continuing education activities and career development for professionals through opportunities to work with ODS.

ODS will continue to offer postdoctoral and career training at its offices. ODS plans to maintain its sponsorship of fellows through the John A. Milner Fellowship with the U.S. Department of Agriculture (USDA) and the American Association for the Advancement of Science Science & Technology Policy Fellowship. ODS will explore other mechanisms to support postdoctoral research training in collaboration with other NIH ICs and federal agencies.

ODS will continue to offer opportunities for academic faculty members to work at ODS during their sabbaticals. Mid- and senior-level faculty members will come to the ODS offices for up to a year to develop experience in investigating dietary supplements and to work with ODS scientists on new initiatives, similar to the new initiative related to iron, for example, that ODS developed with the help of a visiting professor from Cornell University.

Strategy 2-3: Provide funding to stimulate research training in federal laboratories.

ODS will continue to train young intramural investigators in the stimulating environments of research laboratories across the federal government. ODS will maintain its support for the ODS Intramural Research Scholars Program, a one-year competitive scholarship opportunity for NIH intramural junior scientists who have at least one year of postdoctoral research experience. This program will enable them to develop expertise in the scientific exploration of dietary supplements for health promotion and disease prevention.

ODS will maintain its support for interagency agreements to sponsor junior and senior investigators at collaborating federal agencies, such as the National Institute of Standards and Technology (NIST) and the USDA, on projects of mutual interest. An interagency agreement with NIST, for example, supports a postdoctoral fellow in metrology (the science of measurement).

GOAL 3: Foster development and dissemination of research resources and tools to enhance the quality of dietary supplement research.

There is an ongoing need to develop new research methodologies, resources, and tools to support the study of dietary supplements. ODS will continue to coordinate the creation and dissemination of analytical tools for the characterization of dietary supplement ingredients through its Analytical Methods and Reference Materials program (see Program Profile II). This effort will continue to expand beyond dietary supplements to include the measurement of biomarkers of nutrient status in blood and other biological specimens.

Strategy 3-1: Enhance the development of appropriate study methods for dietary supplement research.

ODS will stimulate the development, evaluation, and use of appropriate and rigorous research paradigms for investigating the efficacy and safety of dietary supplements. For example, ODS will continue to support and plan workshops on the latest knowledge and emerging approaches in the study of dietary supplements (similar to the recent workshop on the unique challenges of assessing the safety of botanical dietary supplements).

ODS will support the development of cutting-edge approaches to elucidate the mechanisms of action of complex botanical dietary supplements. The Centers for Advancing Natural Products Innovation and Technology component of the CARBON program develops high-content, high-throughput methods to rapidly generate hypotheses on active compounds and their cellular targets.

ODS will also encourage the development and use of appropriately validated biomarkers of nutrient status in studies of the health effects of dietary supplement ingredients. In addition, through its Population Studies Program, ODS will help to develop tools to evaluate dietary supplement usage more precisely in national health surveys and other large cohorts.

The ability to compare, reproduce, and replicate published research results is essential for building scientific knowledge. ODS will ensure that its co-funded grants adhere to rigorous standards for dietary supplement identification to ensure product integrity using a paradigm established by the NCCIH (<https://ods.od.nih.gov/Research/ProductQualityResources.aspx>). ODS will also continue to promote the highest quality research in dietary supplements by requiring investigators to thoroughly characterize and report the composition of the products they use in mechanistic and clinical investigations.

Strategy 3-2: Foster the highest-quality laboratory analyses for dietary supplement constituents to enhance the quality of dietary supplement products by developing and promoting validated analytical methods and certified reference materials.

NIST is the main producer of reference materials that industry and academia use to ensure precision and accuracy in measurements. ODS will engage stakeholders in identifying needs for

new validated analytical methods and certified reference materials (see Program Profile II). ODS will continue to produce and make available certified reference materials through collaborative interagency activities.

Furthermore, ODS will foster the development, optimization, validation, and use of reliable and accurate analytical techniques for identifying and quantifying specific dietary supplement ingredients and potential contaminants. ODS will support these efforts through funding for research grants, interagency agreements, and contracts with non-government organizations.

Strategy 3-3: Develop and provide publicly accessible databases for use in clinical, epidemiological, and other population research on dietary supplements.

ODS will continue to compile dietary supplement product label information in a publicly accessible database. As it has done since launching the Dietary Supplement Label Database (DSLDD) in 2013, ODS will continue to add dietary supplement product label information to the DSLDD and ensure its reliability. ODS will also continue to call on external experts and request public comments to further enhance the DSLDD by increasing its utility for researchers and consumers.

ODS will continue to prioritize its efforts to analyze ingredients for the Dietary Supplement Ingredient Database (DSID) based on their public health relevance. ODS will also support analyses of ingredients in both foods and dietary supplements to estimate total intakes, especially of key nutrients.

ODS will continue to maintain and enhance the Computer Access to Research on Dietary Supplements (CARDS), its database of federally funded research projects, to cover more years of investment. ODS will also develop a more user-friendly interface and create a more precise and informative research-categorization system for CARDS.

GOAL 4: Translate dietary supplement research findings into useful information for consumers, health professionals, and policymakers.

ODS provides an array of information on dietary supplements and their ingredients that the public views as reliable and up to date. Dietary supplement users will continue to benefit from free access to this objective information. Along with the general public, the website user community includes health care providers and researchers. ODS will continue to collaborate with others in translating research findings into actionable information for public policy and guideline development (see example in Program Profile IV).

Strategy 4-1: Develop and maintain informational resources on dietary supplements for diverse audiences.

ODS will publish new dietary supplement fact sheets (the most viewed materials on the ODS website) and revise existing fact sheets as necessary to keep them current. By 2021, ODS expects to complete fact sheets on all vitamins and minerals. It will also prepare fact sheets on other ingredients in dietary supplement products (such as omega-3 fatty acids) and on dietary supplements for specific purposes (such as to enhance exercise and athletic performance). ODS will continue to create several forms of each fact sheet: a detailed, referenced version directed to health professionals and easy-to-read, "bottom-line" versions in both English and Spanish directed to consumers.

ODS will periodically review and update the ODS website to ensure that it better meets the needs and interests of users. ODS will further increase access to ODS informational resources through various outreach efforts, such as expanding and promoting its service that provides personal responses from ODS nutrition staff to questions about dietary supplements from ODS website users.

Strategy 4-2: Provide leadership on dietary supplement research and educational activities within the federal government.

By congressional mandate, ODS advises the U.S. Department of Health and Human Services and its agencies on matters related to dietary supplements, and it will continue to do so. For example, ODS scientists and the staff of the U.S. Food and Drug Administration's Office of Dietary Supplement Programs will continue to meet by conference call every other month.

To further individual and collaborative efforts on dietary supplement research, education, and communications beyond the Department of Health and Human Services, ODS will continue to lead the Federal Working Group on Dietary Supplements that includes representatives of most NIH ICs and other federal agencies. ODS plans to increase representation on this working group

from additional federal agencies that address dietary supplement issues. Through these efforts, ODS will continue to build strategic partnerships and engage leaders and stakeholders in exchanging information and ideas on nutrition and dietary supplement research, education, and policy.

Strategy 4-3: Collaborate with stakeholders to inform public health policy and clinical practice related to nutrients and other ingredients in dietary supplements.

ODS has enhanced the scientific framework for developing dietary recommendations through the incorporation of systematic reviews into the DRI development process. For example, ODS is supporting a systematic review of the health effects of potassium and sodium (including consideration of levels that may reduce or increase the risk of chronic diseases) and assisting in the coordination of a federal effort to re-examine the DRIs for these nutrients. ODS will continue to promote rigorous evidence-based research for establishing dietary recommendations.

For several years, ODS has conducted an iodine initiative. After convening a series of workshops to identify research needs in this area, ODS is working with other federal agencies to improve assessment of iodine status and measure the iodine content of foods and dietary supplements.

In 2015, ODS established an iron initiative to explore issues surrounding iron during pregnancy, infancy, and early childhood. With the help of federal partners, ODS will convene a public workshop on iron screening and supplementation of iron-replete pregnant women and young children (aged 6–24 months). The workshop will identify the key research needed to address gaps in understanding iron homeostasis in these populations, identify more accurate ways to measure iron status, and determine when iron supplementation is appropriate. ODS will consider the next steps for its iron initiative after the workshop.

Glossary

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| 25(OH)D | 25-hydroxyvitamin D |
| AHRQ | Agency for Healthcare Research and Quality |
| AMRM | Analytical Methods and Reference Materials Program |
| BRC | Botanical Research Center |
| CARBON | Centers for Advancing Research on Botanical and Other Natural Products |
| CARDS | Computer Access to Research on Dietary Supplements |
| CDC | Centers for Disease Control and Prevention |
| CRM | Certified Reference Material |
| DoD | Department of Defense |
| DRI | Dietary Reference Intakes |
| DSID | Dietary Supplement Ingredient Database |
| DSL | Dietary Supplement Label Database |
| FDA | U.S. Food and Drug Administration |
| FTC | Federal Trade Commission |
| ICs | Institutes and Centers [of NIH] |
| IEM | inborn errors of metabolism |
| NHANES | National Health and Nutrition Examination Survey |
| NCCIH | National Center for Complementary and Integrative Health |
| NIH | National Institutes of Health |
| NIST | National Institute of Standards and Technology |
| ODS | Office of Dietary Supplements |
| SRM™ | Standard Reference Material |
| USDA | U.S. Department of Agriculture |
| VDSP | Vitamin D Standardization Program |

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