# *STATUS REPORT: THE FIRST YEARS OF THE OFFICE OF DIETARY SUPPLEMENTS 1995 - 1998*

Office of Dietary Supplements
Office of the Director
National Institutes of Health

# Status Report: The First Years of the Office of Dietary Supplements 1995-1998

## CONTENTS (click on a topic)

# PREFACE

The Office of Dietary Supplements (ODS) was authorized by the Dietary Supplement Health and Education Act of 1994 (DSHEA, Public Law 103-417, Section 13. [a]) (See Appendix A). In late November 1995 the ODS began to function as a small unit within the Office of the Director, NIH to address a list of items that were part of the DSHEA legislation. While the tasks specified for the new office by DSHEA were numerous, the interpretation of how these tasks were to be accomplished was left to the ODS. As first director of the office, I felt it was important to concurrently move forward on as many of the Congressional mandates as possible. I did not want to do so, however, without seeking the advice and counsel of those scientific, government, industry, and advocacy groups who would be working with the ODS and the various communities that were responsible for DSHEA. Therefore, one of the first activities of the ODS was to formally contact professional societies, trade associations, public advocacy groups, and interested government agencies to request recommendations of individuals who could provide advice to the ODS. Through this process the ODS contacted several hundred interested persons who agreed to serve as *ad hoc* advisors and reviewers for the office. Over 150 of these individuals worked with the ODS in developing its strategic plan.

This report presents an overview of the activities of the ODS for its first three years. The items mentioned are nested within the goals and objectives of the strategic plan to illustrate the office's progress in each of these areas. This progress however, would not have been possible without the help of the ODS *ad hoc* advisors who volunteered their time and were involved in nearly all aspects of the work reported here. Their efforts and support have allowed the small staff of the ODS to directly address at some level all of the major Congressional mandates in its first three years. I am extremely grateful for the efforts of the ODS *ad hoc* advisors. It is to these individuals that this report is dedicated!

Bernadette M. Marriott, Ph.D.
Director, ODS
November, 1995 - January, 1999

# OVERVIEW

The Office of Dietary Supplements (ODS) was established by the Dietary Supplement Health and Education Act of 1994 (DSHEA, Public Law 103-417, Section 13. [a]) (see Appendix A) to promote the scientific study of dietary supplements in "maintaining health and preventing chronic disease and other health-related conditions." The DSHEA placed the ODS at the National Institutes of Health (NIH) and mandated specific research and advisory duties. This *Status Report: The First Years of the Office of Dietary Supplements, 1995–1998* describes the activities and accomplishments of the ODS that have been initiated or completed to fulfill its congressional mandates. These activities will be addressed under six headings: Introduction, Foundation, Types of Activities, Accomplishments, Budget, and Conclusion and A Look to the Future.

The **Introduction** presents a brief background and history about why and how the ODS was established by Congress. It includes a description of the ODS staff.

The **Foundation** provides the pertinent sections of DSHEA that define what the ODS must accomplish in general, within the Department of Health and Human Services (DHHS), and within the NIH. The ODS mission statement and an overview of the strategic plan also are described, including the scientific goals and objectives (see Appendix B) that will guide the office's activities.

**Types of Activities** explains the mechanisms that the ODS employs to conduct research, advisory, and educational programs. For example, this section describes the specific types of grants and contracts that the ODS may use to fund research. It also reviews the ways in which the ODS promotes, disseminates, and coordinates research, such as sponsoring scientific workshops and developing databases on dietary supplements.

**Accomplishments** briefly describes the major activities of the ODS since its inception. It includes a review of the process that the ODS used to develop its strategic plan goals. The accomplishments are listed with the scientific goals that are addressed.

The **Budget** section gives a brief review of the ODS budgetary expenditures since 1995.

**Conclusion and A Look to the Future** synopsizes the vision of what the ODS aims to accomplish in the near future.

# INTRODUCTION

## Background

A national survey conducted in 1992 by the National Center for Health Statistics reported that approximately 50 percent of the respondents took dietary supplements in the previous year, and about half of those did so on a daily basis (Slesinski, et al.1995). National sales of dietary supplements in 1998 totaled almost $12 billion, which is projected to increase to over $14 billion by the year 2000 (Aarts, 1998). Dietary supplements have been defined by DSHEA (Public Law 103-417, Section 3. [a], October 1994) to include

> a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: (A) a vitamin; (B) a mineral; (C) an herb or other botanical; (D) an amino acid; (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E).

For many dietary supplements, scientific studies of dosing, efficacy, safety, and biological mechanisms of action (Lewis and Hohl, 1997) are limited or nonexistent. Of additional public health concern is the potential for unfavorable interactions of self-administered dietary supplements with prescription medication and/or nutrient absorption from the diet. Consumers have voiced concern about the validity of supplement advertisements and have questioned where they can turn for credible, scientifically based information. Identification of gaps in scientific knowledge, the promotion and support of research needed to fill these gaps, and dissemination of science-based information on dietary supplements to health care practitioners and the public are the main goals of the ODS.

## Brief History

The ODS was established at the National Institutes of Health (NIH) by the Dietary Supplement Health and Education Act of 1994 (DSHEA) (Public Law 103-417, Section 13. [a]) (see Appendix A). This law was passed “to set standards with respect to dietary supplements.” The DSHEA specified seven major purposes and duties for the ODS and its director, including to promote the scientific study of dietary supplements “in maintaining health and preventing chronic disease and other health-related conditions.”

Beginning in early 1995, William R. Harlan, M.D., Associate Director for Disease Prevention, NIH, met with professional, scientific, and trade organization representatives interested in dietary supplements to determine the state of the science. He also initiated preliminary investigations into methods for developing several dietary supplement research databases that are specified in the DSHEA.

In November 1995, the ODS began formal operations when Bernadette M. Marriott, Ph.D., was appointed Director of ODS by Harold E. Varmus, M.D., Director of NIH. Early in 1996, Dr. Marriott began promoting open dialogue among scientists, academicians, government

representatives, and industry regarding dietary supplements and encouraged these groups to actively contribute to the strategic planning process of the ODS. Dr. Marriott also met with the Institute and Center (IC) directors at NIH to introduce them to the purpose and activities of the ODS, as well as to identify common areas of scientific interest. These meetings helped to create relationships with the ODS that have subsequently led to collaborations on the variety of scientific activities that are described in this report.

Although the DSHEA authorized a budget of $5 million with which to carry out its mandated duties, these funds have not been appropriated. Therefore, the initial costs of the ODS for 1995 were funded through the NIH Director's Discretionary Fund. Since fiscal year (FY) 1996, the operating and program funds for the ODS have been a line item in the budget of the NIH Office of the Director.

## ODS Staff

Bernadette Marriott, Ph.D., Director, came to the ODS at its inception in November 1995 from the Food and Nutrition Board (FNB), Institute of Medicine (IOM), National Academy of Sciences (NAS), Washington, D.C., where she was Deputy Director, responsible for planning and managing the research evaluation of national and international food and nutrition. Dr. Marriott received a Ph.D. in Experimental Psychology in 1979 from King's College, University of Aberdeen, Scotland. She subsequently obtained additional research training in comparative medicine and trace mineral nutrition at the Johns Hopkins University School of Medicine. Her B.Sc. degree, in biology/immunology, is from Bucknell University, Lewisburg, Pennsylvania. Having served as a Peace Corps volunteer from 1970 to 1972 at the University of Mashhad, Iran, Dr. Marriott has also lived and worked outside the continental United States in Scotland and Puerto Rico and has conducted field research and taught in Afghanistan, Nepal, Panama, Puerto Rico, and Thailand. Before taking a staff position at the FNB in 1990, she served as staff officer for the Institute of Laboratory Animal Resources, NAS. Prior to that, she held faculty positions at the Johns Hopkins University Schools of Medicine and Public Health, the University of Puerto Rico School of Medicine where she was co-appointed as Associate Director for Education and Associate Scientist at the Caribbean Primate Research Center, and at Goucher College.

Dr. Marriott's background includes broad research experience focusing on natural food supplementation and micronutrient requirements in human and nonhuman primates. Her studies have focused on the long-term feeding habits of nonhuman primates in natural habitats and in the laboratory. She has conducted much of this work in collaboration with scientists at the U.S. Department of Agriculture (USDA) Human Nutrition Center in Beltsville, Maryland.

At its inception, the ODS had no staff other than the director. A number of short-term, temporary, and contractual employees have been instrumental in moving the activities of the ODS forward. In January 1996, Marcia Ancker joined Dr. Marriott as a temporary secretary. To begin developing the Congressionally mandated functions of the office, Rebecca Erickson was hired on contract in summer 1996 to oversee the design and development of the databases. Also during the summer 1996, the ODS benefited from the assistance of two graduate students, Eric Manheimer and Caroline Chung. Eric continued with the ODS through 1997 on various research and research support projects. In September 1996, Pamela Dressell joined the staff on a part-time, six-month detail from the Veterinary Resources Program, National Center for Research Resources, NIH. Ms. Dressell is a communications specialist who assisted the ODS with developing outreach efforts and the ODS logo. In 1997, Ellen Nayeri, a specialist in library

science, assisted the ODS in developing its bibliographic database, identifying information resources, and structuring the ODS resource document management system. Jeanette M. Hosseini, Ph.D. and Judy H. Pruden, from the NIH Clinical Center and the Centers for Disease Control and Prevention (CDC), respectively, assisted the ODS through short-term assignments. Meredith Robbins participated with the ODS during the summer 1998 as a student intern. Leslie Collier provided secretarial support beginning in 1998. Also during that time, Donna Allen was contracted as a manuscript specialist and to coordinate the publication of conference proceedings.

Terri Krakower, Ph.D. is the scientific communications specialist for the ODS and the coordinator of the IBIDS database. Dr. Krakower joined the ODS staff in May 1998 on a contractual basis to compile this status report and to analyze, coordinate, and finalize the writing and review of the ODS strategic plan. Her background includes research on two cancer projects and identifying molecular interactions within the protein-making machinery of the cell. Dr. Krakower received a Ph.D. in biochemistry from the University of Texas at Austin where she was a predoctoral fellow in the Institute for Neuroscience Research. Her research was focused on enzymes that have been implicated in alcoholism, depression, and Parkinson's disease. Dr. Krakower also received extensive graduate training in nutrition at the University of California at Davis after she received her B.S. degree in biochemistry and biophysics.

Rebecca Bortz Costello, Ph.D. was appointed as nutrition scientist in July 1998. Dr. Costello has extensive training in the nutritional management of cardiovascular diseases and most recently served as Study Director with the FNB, NAS in the area of nutrition policy. Her work focused on evaluating the nutritional adequacy and use of nutritional supplements for sustaining and enhancing performance in military personnel. She was also involved in developing programs to assess the quality of clinical and nutrition care services and to examine the relationship between alcohol and overall diet. Dr. Costello received her doctorate in clinical nutrition from the University of Maryland at College Park and has taught at the graduate and undergraduate levels. She has worked with patients as a clinical nutrition specialist and coordinated a series of clinical drug studies that investigated therapies for cardiovascular disease.

Christine Swanson, Ph.D. was appointed as a nutrition scientist in November 1998. Dr. Swanson received her undergraduate training in dietetics at Montana State University in Bozeman. She received her M.P.H. and doctorate in nutritional sciences from the University of California at Berkeley. She did postdoctoral work with the USDA Human Nutrition Research Center in Beltsville, MD and also worked for Nestle Research, Switzerland. Initially Dr. Swanson conducted human metabolic studies of zinc and selenium. More recently, she conducted research in the Division of Cancer Epidemiology and Genetics at the NCI. Her epidemiologic research focused on studies of the relation of alcohol, body size and cancer risk. Dr. Swanson has taught nutritional epidemiology to clinicians at the University of Indonesia, Jakarta.

# FOUNDATION

## Congressional Mandates

The DSHEA designated general scientific functions and duties for the ODS, as well as specific tasks for the office and its director. These mandates are stated below as they apply to the ODS in general, within the Department of Health and Human Services (DHHS), and within the NIH. The complete provisions of DSHEA that are applicable to the ODS are included in Appendix A.

**ODS General Mandates**

The DSHEA identified two broad functions for the ODS:

- "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; and
- to promote scientific study of the benefits of dietary supplements in maintaining health and preventing chronic disease and other health-related conditions. . . . "

**ODS Mandates within the DHHS**

As the principal federal agency responsible for protecting and promoting the health of Americans, the mission of the DHHS includes "fostering strong, sustained advances in the sciences underlying medicine, public health, and social services" (DHHS, 1997). The ODS has a dual mandate to provide scientific support related to dietary supplements within the DHHS:

- "compile a database of scientific research on dietary supplements and individual nutrients;
- . . . serve as the principal advisor to the Secretary and to the Assistant Secretary for Health and provide advice to the Director of the National Institutes of Health, the Director of the Centers for Disease Control and Prevention, and the Commissioner of Food and Drugs on issues relating to dietary supplements. . . ."

**ODS Mandates at NIH**

ODS also has specific mandates within the NIH. As the major funding agency of biomedical research in the United States, the NIH has a leadership role in setting the agenda for scientific research and policy (NIH, 1997). The DSHEA charged the ODS with a threefold mandate within NIH, to:

- "conduct and coordinate scientific research within the National Institutes of Health relating to dietary supplements and the extent to which the use of dietary supplements can limit or reduce the risk of diseases such as heart disease, cancer, birth defects, osteoporosis, cataracts, or prostatism;
- collect and compile the results of scientific research relating to dietary supplements, including scientific data from foreign sources or the Office of Alternative Medicine;
- . . . coordinate funding relating to dietary supplements for the National Institutes of Health."

## Strategic Plan and Mission Statement

The ODS strategic plan, *Merging Quality Science with Supplement Research, A Strategic Plan for the Office of Dietary Supplements* (ODS, 1998) (see Appendix B for executive summary), sets the future course of scientific activities for the ODS for the next three to five years. As part of the planning process, an **operating definition of dietary supplements** was developed to aid scientists and administrators in identifying whether the compounds of interest to them are within the ODS mandate. The ODS **mission statement** and **five scientific goals** and **objectives** to realize these goals were also enumerated. The goals and objectives were chosen to address the most relevant scientific and public health issues in the field of dietary supplements, as well as to identify areas in which the ODS is likely to make unique contributions. The basic **operating principles** for all ODS activities include supporting the highest quality science and addressing issues of safety and efficacy of dietary supplements. **Criteria** were identified to facilitate decision making among competing scientific priorities. Lastly, mechanisms were established to identify and respond to unanticipated and **emerging science** issues and to maintain the plan's effectiveness through a **strategic plan evaluation process**.

One outcome of the strategic planning process was the development of a succinct ODS mission statement that reflects the ODS purpose and mandates.

### ODS Mission Statement

**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**.

# TYPES OF ACTIVITIES

Through the strategic planning process, the ODS determined five scientific goals and associated objectives that are most relevant to the field of dietary supplements (see Appendix B). The types of activities that the ODS uses to address and accomplish these goals and objectives are described below. They are categorized according to research support, research promotion and dissemination, research coordination, advisory duties, and education.

## Research Support

One of the major duties mandated by the DSHEA is to "conduct and coordinate scientific research within the National Institutes of Health relating to dietary supplements and the extent to which the use of dietary supplements can limit or reduce the risk of disease." The NIH "places a high priority on funding basic research" (NIH, 1997). Therefore, a majority of the total NIH budget is devoted to funding biomedical research and research training. For example, in FY 1996, 83 percent of the total NIH budget was spent on research funding and training (NIH, 1997).

As part of the NIH, the ODS devotes the majority of its budget to funding research. As a trans-NIH office located within the Office of the Director, the ODS does not have the authority to directly fund investigator-initiated research grant applications. The ODS, therefore, conducts research by providing support for grant applications to scientific investigators through joint endeavors with the Institutes and Centers (ICs) at NIH or other government agencies. The ODS typically funds research through grants and contracts. The specific types of grant and contract mechanisms used by the ODS are detailed below.

Numerous resources are available that provide more detailed information for investigators and the public about the current funding programs and policies at NIH. The *NIH Guide for Grants and Contracts* is the official document that describes all of the research, research training, and contracting opportunities. It is available electronically through the NIH Internet home page (http://www.nih.gov/grants/). Publications such as the *Catalog of Federal Domestic Assistance* and *The NIH Extramural Programs: Funding for Research and Training,* describe the current scientific program areas at the NIH. Descriptions of the various grant classifications as well as the mission statements and areas of interests of the ICs and offices may also be accessed via the World Wide Web (http://www.nih.gov/grants/policy/emprograms). Specific information about grant programs and application procedures may also be obtained from the Extramural Outreach and Information Resources Office, within the Office of Extramural Research, NIH.

### Grants

Research grants are awarded to nonprofit institutions and organizations, government agencies, individuals, and commercial organizations for the support of scientific research. Grants provide the funds to conduct research, including the salaries of scientists and technicians, equipment, supplies, and other associated costs of research such as library services and building maintenance. The duration of grant awards is typically from one to five years.

Research project grants are the largest category of funding provided by the NIH (NIH, 1997). Most grant applications are investigator-initiated, which means that the applicant develops the research concepts, strategy, and methodology and then proposes a research project or training activity that is relevant to the stated mission and goals of one or more of the ICs.

Applications for grants are mandated by law to undergo two sequential levels of peer review. First, the scientific merit is evaluated by a scientific review group comprising nongovernment scientists with demonstrated knowledge and competence in a relevant scientific or medical specialty. Second, the overall merit is evaluated by national advisory boards or councils that include eminent scientists and the members of the public. These groups also consider policy issues, such as the project's relevance to specific program goals and available funding.

The ODS funds research grants to scientific investigators at universities, medical schools, hospitals, small businesses, and research institutions by intra- or interagency agreements with the ICs at the NIH or with other federal agencies. One example of an intraagency agreement that the ODS utilizes to support research on dietary supplements is the **Research Enhancement Awards Program (REAP)**. Through REAP, grant applications are received and reviewed by the ICs according to the standard NIH grant process for extramural research. Highly meritorious applications that fall outside an IC's funding resources and are within the research interests of ODS can be nominated by NIH ICs to receive partial or full funding from ODS. This innovative and successful program was originally designed by the NIH Office of Research on Women's Health. The ODS has funded 13 REAP awards that are described in the "Accomplishments" section of this report (see also Appendix C).

To encourage the submission of grant applications in key scientific areas, the ODS may initiate **Program Announcements (PAs)** or **Requests for Applications (RFAs)** jointly with the ICs or other federal agencies. The NIH generally identifies these key areas, as well as gaps in scientific knowledge that need to be addressed, by gathering the opinions of outside experts through conferences, workshops, and symposia (see Research Promotion and Dissemination). A PA is a formal statement issued to describe a new, expanded, or continuing scientific program. Grant applications responding to PAs can be submitted on an ongoing basis. A RFA is a formal request for grant or cooperative agreement applications that address specific scientific objectives and there is a commitment of support for meritorious grants. With the RFA mechanism, there is usually a cooperative endeavor among grantees and the Institute(s). RFAs usually have a one-time application deadline and review.

**Research Centers**

Developing and supporting research centers is one mechanism that NIH can use to fund broad research programs on a range of biomedical problems with a central theme. A research center is a group of collaborating scientists who have demonstrated expertise in conducting research on a specific topic and who concentrate their efforts on a common research problem. The investigators may be from the same scientific discipline, but they often are from different disciplines, which provides a multidisciplinary approach to the various aspects of the study. Center investigators may be from one or many collaborating institutions. Often, centers are based at universities; however, they may include other facilities, such as local hospitals, animal care units, or computer resource units.

Research centers are generally developed in response to specific programmatic needs of an IC and have a research theme. Centers receive ongoing involvement from NIH staff. Funding

for centers can support the full continuum of research activities, which includes basic and applied research as well as clinical applications. Centers provide shared resources, facilities, and expertise for the combined research endeavor and thus aim for increased productivity and efficiency. Centers may also be created to provide a local or national resource for a specific purpose.

The ODS believes that there is a need to establish Centers for Dietary Supplement Research Centers in order to effectively fulfill its congressional mandate to promote dietary supplement research. The ODS seeks to collaborate with the NIH ICs, other government agencies, and industry to jointly develop and fund research centers that will focus on the efficacy and safety of dietary supplements.

**Contracts**

Contracts are a mechanism that the U.S. government uses to procure basic, applied, and clinical biomedical research services where a specific need has been identified. The research is generally solicited through dissemination of **Request for Proposals (RFPs)**.

RFPs contain the information needed to prepare a contract proposal, including a detailed statement of work, expected performance schedule, and criteria that will be considered for making the award. Research that is funded from contracts differs from research funded by grants, in that it is NIH-initiated rather than being investigator-initiated, and the NIH exercises direction or control through the statement of work and by monitoring the technical performance. The NIH ICs are responsible for administering contracts in conjunction with the NIH Office of Contracts Management. Proposals that respond to RFPs undergo review for their technical merit, including the past performance of the applicant on similar projects, and for their financial aspects. All of the criteria used to evaluate the proposals and their relative importance are described in the RFP.

It is the policy of NIH to advertise RFP opportunities as widely as possible to increase competition for these awards. Generally, all RFPs issued by NIH are published in the *Commerce Business Daily* (obtained from the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9371). RFPs are also shown in the *NIH Guide for Grants and Contracts* (from the Office of Extramural Outreach and Information Resources, NIH, 6701 Rockledge Drive MSC 7910, Bethesda, MD 20892-7910, telephone 301-496-5366, fax 301-480-8443). This document may be accessed through the NIH web site (http://www.nih.gov), which allows the reader to download the RFPs electronically. The NIH web site also posts *A Guide to the NIH Contracting Process,* which provides potential applicants with information on how to submit proposals, how proposals are evaluated, and answers to frequently asked questions.

ODS will use RFPs to stimulate scientific research in the field of dietary supplements, particularly in the priority areas identified in *Merging Quality Science with Supplement Research, A Strategic Plan for the Office of Dietary Supplements* (ODS, 1998). The ODS can initiate contracts and collaborate with other federal agencies such as the Centers for Disease Control and Prevention, the Food and Drug Administration, the Department of Defense, and the U.S. Department of Agriculture.

**Partnering Programs**

To encourage small business participation in innovative research and development (R&D) and to increase the commercialization of the resulting technologies, in 1982 Congress enacted Public Law 97-219, the *Small Business Innovation Development Act*, and Public Law 102-564, the *Small Business Research and Development Enhancement Act of 1992*. As a result,

the DHHS, including NIH and other federal agencies, are required to set aside a designated percentage of their R&D budgets for the programs that are described below. Because the start-up and development phases for innovative technologies can be risky and quite expensive, these grants enable qualified small businesses to be competitive in high-technology industry. A small business is a for-profit organization that has its principal place of business in the United States, is not dominant in its field, and has no more that 500 employees.

The **Small Business Innovation Research (SBIR)** program provides funding to small businesses to support innovative technological research that is likely to result in commercial products or services. In FY 1998, the set-aside fund for SBIR at NIH was $264.7 million, which represents a substantial increase from the previous year.

The **Small Business Technology Transfer Research (STTR)** program provides grants for research that is conducted by a small business in cooperation with a nonprofit research institution. The small business and the research institution must conduct at least 40 percent and 30 percent of the research project, respectively. During FY 1998, the STTR program of NIH had $15.9 million available, which also represented an increase from the previous year.

SBIR and STTR grant applications at NIH are mandated by law to undergo peer review. Because these projects are usually highly scientific, they are reviewed by a panel of scientists who are expert in the relevant scientific field. Some of the factors that are evaluated during the scientific review are the qualifications of the business, degree of innovation, technical merit, and the potential for commercialization. The projects are divided into three-phases: (1) the start-up phase which establishes the feasibility of the idea; (2) the in-depth R&D phase, which includes evaluation of the commercial potential of the technology; and (3) the final phase which moves the innovation into the marketplace. SBIR and STTR grants do not support the third phase; therefore, private or other federal funding must be obtained.

The NIH web site offers detailed information about SBIR and STTR programs, downloadable applications, the criteria for review, and an overview of the types of grants that have been funded by NIH in previous years (http://www.nih.gov/grants/funding/sbir.htm). One particularly useful site is “Advice and Information on SBIR and STTR Programs” (http://deainfo.nci.nih.gov/awards/sbir_sttr/sbir_nih.htm), which presents advice and mentoring for applicants, including writing tips, descriptions of the peer review process, and a comparison of the SBIR and STTR programs. The federal government also sponsors regularly scheduled conferences at different locations nationwide to assist applicants with understanding the SBIR and STTR programs and how to apply. Schedules and locations of the current conferences can be found at the National SBIR Conference Center web site (http://www.zyn.com/sbir/).

The ODS encourages corporate groups and academic institutions to form partnerships and apply for SBIR and STTR grants related to dietary supplements and the technology needed to understand the mechanisms of action of dietary supplement ingredients. These programs provide an ideal opportunity for supporting research and development of new technologies and programs. The role of the ODS in the SBIR and STTR programs, in general, is to facilitate and coordinate the development of such partnerships with the NIH ICs.

**Gift Fund**

A gift fund at NIH is an account that is supported by donations or bequests; it is a separate account from the appropriation that NIH receives from Congress. As part of the NIH, the ODS can accept donations and bequests to support the mission of the office. These funds support research in general and cannot, therefore, be earmarked for specific projects or

investigations. However, gift funds may be categorically specified for use in broad types of research, such as vitamin, mineral, or botanical supplement research. More specific information can be found on the ODS web site.

## Research Promotion and Dissemination

A primary purpose of the ODS, specified in the DSHEA, is to promote the scientific study of the potential role of dietary supplements in maintaining health and reducing the risk of chronic disease. To fulfill this congressional mandate, the ODS participates in the types of activities described below. Some of these activities are performed independently and others are performed collaboratively with the NIH ICs.

### Conferences, Workshops, and Symposia

Large conferences or workshops are organized to bring together scientists and professionals from different scientific disciplines in order to provide an overview of a topic, as well as to identify gaps in research and directions for future research. Smaller sessions are also held to convene scientists who are actively working in one field of research so that they can have intensive dialogue on a specific topic.

To stimulate research, the ODS plans, organizes, and supports small conferences, workshops, and symposia on scientific topics related to dietary supplements. The ODS can initiate such activities alone, but more often it collaborates with NIH ICs, other governmental agencies, and professional organizations in scientific areas of mutual interest. Occasionally, the ODS sponsors large conferences or workshops in fields related to dietary supplements. In 1996 and 1998, the ODS initiated two major workshops that were co-sponsored by numerous NIH ICs as well as external organizations. They were *The Role of Dietary Supplements for Physically Active People* and *Zinc and Health: Current Status and Future Directions*. A complete list of workshops and conferences that the ODS has organized or co-funded is given in Appendix D.

In 1997, the ODS initiated the innovative **ODS Conference Grant Program** (CGP) to stimulate research on dietary supplements, which is similar to a highly successful program of this nature originated by the NIH Office of Rare Diseases. The program is made possible through an annual set-aside fund to support NIH IC-initiated scientific conferences, workshops, or symposia. Primary consideration for support is given to sessions that deal with those dietary supplements or groups of supplements for which current research is lacking or lagging or if the likely outcome of session(s) would be the stimulation of research. In addition, consideration is given to a session on supplements for which the data appear conflicting or where a highly focused scientific workshop might clarify research findings and gaps in science. The conferences sponsored by this initiative are included in Appendix D.

### Publications

Publications are an important mechanism for promoting scientific research and disseminating research findings. The ODS publishes **scholarly reviews** about dietary supplements in peer-reviewed scientific journals. In addition, the ODS prepares for the public dietary supplement **fact sheets** that are derived from the reviews and that interpret the literature findings in a more applied sense. To disseminate the most current research findings, the ODS also publishes the **proceedings** from some of the major workshops it sponsors. The proceedings

are usually published in a scientific journal as a supplement dedicated to the topic of the workshop. Formal **bibliographies** are often prepared for the workshops in conjunction with the National Library of Medicine. The bibliographies serve as a resource for researchers and for workshop participants, to inform them in areas that are related to their specialty, but distinct from it. Current ODS publications are accessible through the ODS Internet web site and are listed in Appendix E.

**Databases**

Databases are computerized systems of information that can be accessed and searched for specific topics. For example, databases exist that provide scientific literature citations, DNA and protein sequences, chemical carcinogens, as well as administrative databases of goods and services. Reports can be generated by searching the database, for example, to produce a list of publications or clinical trials dealing with a specific topic.

Congress mandated that the ODS collect and compile databases of federally funded research and peer-reviewed scientific literature regarding dietary supplements. To fulfill these mandates, the ODS is developing two databases that will be accessible to the public through the ODS Internet home page. **IBIDS** (International Bibliographic Information on Dietary Supplements) is a database of published, international, scientific literature on dietary supplements that is accessible to the public through the ODS Internet home page (http://dietary-supplements.info.nih.gov/databases/ibids.html). **CARDS** (Computer Access to Research on Dietary Supplements) is a database that will consist of existing and ongoing dietary supplement research currently supported by federal agencies. IBIDS and CARDS are described in detail in the "Accomplishments" section of this report.

**Internet Home Page**

One of the most effective and inexpensive methods for accomplishing widespread communication is the use of information technologies such as the World Wide Web. The ODS developed an Internet home page to disseminate information. This web site (http://dietary-supplements.info.nih.gov) is another avenue for coordinating research efforts and support in dietary supplements at NIH. A primary goal during its development was to ensure that the format would be easy to use and would provide quick information access by a broad spectrum of individuals, including scientists, health care professionals, the industry, educators, the media, and the general public.

The ODS web site provides information on the ODS, including its origins, mandates, mission statement, and strategic plan. It also provides access to the ODS databases and publications, current funding opportunities, as well as other activities, programs, and scientific resources. Other World Wide Web sites that are relevant to dietary supplements are linked to the ODS home page, including sites at NIH and other federal agencies; dietary supplement-related databases; scientific, professional, and trade association organizations, and other links of interest.

The ODS web site will be a dynamic, evolving project that will be enhanced and updated as information becomes available, as the needs of users change, and as new discoveries about dietary supplements are revealed through research.

**Awards of Merit**

Awards of merit are monetary awards that may be given to scientists or staff to recognize outstanding efforts on behalf of the ODS. Travel awards may also be given to defray the cost of

scientists' attendance at a conference co-sponsored by the ODS. **Promising New Investigator Awards** are funded by the ODS as part of its effort to promote research in dietary supplements. Through these awards, the ODS encourages scientists to continue research in dietary supplements by recognizing their achievements and by providing support for participation in conferences that provide a state-of-the-art review of current dietary supplement research. Various mechanisms, including intra/interagency agreements, are used to implement these awards. In 1998, the ODS provided Promising New Investigator Awards to defray the cost of attendance at a conference co-sponsored by the ODS, "Nutritional and Health Benefits of Inulin and Oligofructose", to five scientists whose research was related to the conference. Two **On-the-Spot Awards** of merit were also given to NIH staff members for their contributions to specific ODS activities.

## Research Coordination

To coordinate research and funding on dietary supplements at the NIH, the ODS has established a **Dietary Supplements Liaison Panel**, which consists of members appointed by the directors of the ICs at the NIH. This group meets periodically to identify fruitful areas for joint research and to coordinate those research efforts. The liaison group is currently developing a mechanism for trans-NIH research coordination on dietary supplements.

The ODS also serves as a member of the NIH **Nutrition Coordinating Committee** (NCC), which is managed through the NIH Division of Nutrition Research Coordination, National Institute of Diabetes and Digestive and Kidney Diseases. The NCC coordinates all nutrition research at NIH and provides a regular forum for dialogue among ICs about scientific issues related to nutrition, diet, and health. In addition, the NCC staff provides a link to the DHHS interagency Nutrition Policy Board, which coordinates nutrition research among the public health agencies and the Interagency Committee on Human Nutrition Research (a subcommittee of the Committee on Health, Safety and Food of the National Science and Technology Council in the Office of the President).

## Advisory Duties

The ODS is mandated to serve as principal adviser to the Secretary and Assistant Secretary for Health, as well as advise the NIH Director, the CDC Director, and the Commissioner of Food and Drugs about issues related to dietary supplements. The ODS fulfills this mandate by answering **inquiries**, writing **reports**, delivering **presentations**, and participating in **interagency committee** activities on a regular basis. The ODS also provides advice to Congress on request related to dietary supplements.

## Education

Part of the mission of NIH is "fostering communication of biomedical information." Within the Office of the Director is the Office of Science Education, among whose activities

include “developing curriculum supplements and other educational materials related to medicine and research through collaborations with scientific experts at NIH.”

One of the goals of ODS is to inform and educate scientists, health care professionals, and the public about the benefits and risks of dietary supplements. Therefore, the ODS initiates and participates in educational and training activities related to dietary supplements. Some examples of these are: **grantwriting** workshops for scientists and professionals to promote the submission of competitive grant proposals, dietary supplement **education modules for medical schools**, and peer-reviewed **fact sheets** to help the public interpret the scientific literature.

# ACCOMPLISHMENTS

In its first three years, the ODS has made significant progress in addressing the congressional mandates specified in the DSHEA. One purpose mandated by DSHEA is for ODS "to promote scientific study of the benefits of dietary supplements in maintaining health and preventing chronic disease and other health-related conditions." From the outset, the ODS Director made a commitment to incorporating the Department of Health and Human Services (DHHS) customer service plan into all ODS activities. This plan strives to provide standards of quality and customer service within government that equal the best in the private business sector. This approach has guided the development of the ODS strategic plan, as well as all other activities undertaken by the office. The major accomplishments of the ODS from 1995 through spring 1998 are described below.

## Incorporation of DHHS Customer Service Plan

Shortly after the ODS was authorized, Secretary Donna E. Shalala, DHHS, integrated new customer service standards into the agency's mission "to protect and promote the health, social, and economic well-being of all Americans in a way that provides the highest quality service." This customer service plan, authorized in August 1995, was in response to Executive Order 12862, "Setting Customer Service Standards," which called for the federal government to become customer-driven in order to achieve the finest standards of quality for the American people. Each agency was to develop, publish, and make readily available to the public its own customer service plan with specific standards of performance.

The ODS has adopted the DHHS customer service philosophy and has incorporated it into its own operating plan. Its commitment to this approach was demonstrated through a strategic planning process in which ODS convened a series of seven cross-cutting planning meetings comprised of representatives from the public, government, industry, and scientific communities (see Development of Strategic Plan and Mission Statement). During these meetings, the ODS sought input regarding the development of its mission statement, scientific priorities, and strategic plan. Continuing this approach, the ODS maintains an open dialogue with its constituents regarding all ODS activities and has striven to cultivate effective partnerships that will promote scientific excellence and benefit the health of the American public.

## Establishment of Ad Hoc Advisory Group

During the first year of its operation, a principal goal of the ODS was to inform the biomedical, professional, and industry communities about the new office and to begin forging partnerships for future scientific activities. The ODS Director maintained an intensive agenda that included delivering more than 35 presentations at national and international scientific and public meetings. Each presentation included a request that individuals from academia, industry, government, and the public participate in the development of the ODS strategic plan. Professional groups were identified that represented the major scientific and public interests in the field of dietary supplements. These groups were then formally requested to recommend

individuals who were knowledgeable about the scientific and public issues related to dietary supplements. These individuals were subsequently invited to participate as *ad hoc* advisers to the ODS. Over 98 percent of those contacted accepted the invitation. The *ad hoc* advisers provide scientific and technical suggestions and guidance regarding office programs and planning.

## Development of Strategic Plan and Mission Statement

As a new office within the NIH, the ODS was faced with numerous decisions that would affect the future direction and success of the office. Therefore, in an effort to progress systematically and deliberately, the ODS determined that a coherent strategic plan was necessary to guide decision making. The strategic plan was designed with well-defined, short- and long-term goals that can be evaluated and improved. It was also designed to be dynamic; it will be evaluated at regular intervals to assess the effectiveness of the strategies and methods used to achieve the ODS goals and objectives. This evaluation process also provides opportunities for making adjustments in response to unanticipated scientific opportunities or public health needs.

Seven strategic planning meetings were held from September 1996 through February 1997. The meetings involved over 150 scientists and professionals from academia, industry, government, and public interest groups. The first three meetings, each attended by a different set of specialists, focused on the definition and scope of dietary supplements and began to identify the most significant issues for the ODS to address as scientific priorities. The next three meetings involved additional unique groups of *ad hoc* advisers and built on the first phase to develop a mission statement, further define scientific priorities, and identify specific activities for the ODS.

The collective input from these groups was used to develop a preliminary draft of the ODS strategic plan. At the seventh meeting, the ODS convened representatives from the NIH ICs and other interested federal agencies to review and critique the preliminary draft. Comments on the preliminary draft, coupled with comments and suggestions from the earlier sessions led to a final draft of the ODS strategic plan. This draft was sent to all strategic planning participants for their review and comments. Over 700 of the comments, concerns, and suggestions were received, carefully reviewed by the ODS staff, and incorporated into the final ODS strategic plan, *Merging Quality Science with Supplement Research, A Strategic Plan for the Office of Dietary Supplements* (ODS, 1998) (see Appendix B for executive summary).

## Accomplishments Listed by Scientific Goal

Five equally weighted nonprioritized goals were established in the ODS strategic plan, *Merging Quality Science with Supplement Research, A Strategic Plan for the Office of Dietary Supplements* (ODS, 1998):

Goal 1: Evaluate the role of dietary supplements in the prevention of disease and reduction of risk factors associated with disease.
Goal 2: Evaluate the role of dietary supplements in physical and mental health and performance.
Goal 3: Explore the biochemical and cellular effects of dietary supplements on biological systems and their physiological impact across the life cycle.

Goal 4: Advance scientific methods in the study of dietary supplements.
Goal 5: Inform and educate scientists, health care providers, and the public about the benefits and risks of dietary supplements.

The major activities of the ODS during its first years of operation, 1995 through fall 1998, are listed under the scientific goals that they support. Scientific publications and presentations that have resulted from the supported projects are given after the project description.

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

### ACTIVITIES IN PROGRESS:

***Chronic Dental Disease and Cardiovascular Disease,* A Scientific Study**

The National Institute of Dental and Craniofacial Research and the ODS are co-sponsoring a project at the Harvard University School of Dental Medicine that will examine the epidemiological relationship between oral health, coronary heart disease (CHD), and stroke. Researchers are exploring two possible mechanisms for the association: (1) that chronic dental infection could lead to increased levels of biomarkers known to be associated with CHD, and (2) that tooth loss could result in dietary changes that may be associated with increased risk of CHD. The study will examine dental health, diet, and nutrient supplement consumption data obtained from 51,529 men and 90,000 women enrolled in ongoing studies funded by the National Cancer Institute, the National Institute on Alcohol Abuse and Alcoholism and the National Heart, Lung, and Blood Institute. This study has the potential to provide important new approaches for the early identification of risk factors, particularly dental health, that may help in the prevention of CHD and stroke. Starting date: 1998.

***Role of Antioxidants in Preventing Cataract Development in Persons with Diabetes,* A Scientific Study**

The National Eye Institute and ODS are co-sponsoring a project at the University of Texas Medical Branch in Galveston to examine the role of antioxidants in preventing cataract development in persons with diabetes. A key aim of this study is to determine if antioxidants can prevent the production of specific toxic compounds found in the lens of the eye affected by diabetes. Starting date: 1997.

Publications and presentations from this study:

- Ansari, N.H., Zhang, W., Fulep, E. and Mansour, A. (1998) Prevention of pericyte loss by trolox in diabetic rat retina. *J. Toxicol. Environ. Health*. 54:467–475.
- Ansari, N.H., Zhang, W., He, Q., Andley, U., Zhou, F. and Thompson, E.B. (1998) Enal-induced apoptosis in human lens epithelial cells (HLECs). XIII International Congress of Eye Research, July 26–31, Paris, France.
- He, Q., Khanna, P., Srivastava, S., van Kuijk, F.J.G.M. and Ansari, N.H. (1998) Reduction of 4-hydroxynonenal and 4-hydroxyhexenal by retinal aldose reductase. *Biochem. Biophys. Res. Comm*. 247:719–722.
- Zhang, W., He, Q., Andley, U., Zhou, F., Thompson, E.B. and Ansari, N.H. (1998) Induction of apoptosis by lipid peroxidation products in human lens epithelial cells. Poster presentation at the Thomas N. James-Sealy Symposium, April 5–6, Galveston, TX.

- Zhang, W., Lie, Q., Campbell, G.A., Chan, L.L., Thompson, E.B. and Ansari, N.H. (1998) Enal-induced apoptosis: A mechanism of oxidative injury. Poster presentation at the Environmental Health Poster Presentations, March 17, Galveston, TX.
- He., Q., Wang, L., Srivastava, S.K. and Ansari, N.H. (1998) Role of lipid-derived aldehydes in cataractogenesis. Poster presentation at the Environmental Health Multidisciplinary Research Presentations, March 17, Galveston, TX.
- Khanna, P., Wang, L., Perez-Polo, R.J. and Ansari, N.H. (1997) Oxidative defense enzyme activity and mRNA levels in lenses of diabetic rats. *J. Toxicol. Environ. Health.* 51:541–555.
- Zhang, W., Chan, L.L., Thompson, E.B. and Ansari, N.H. (1997) Lipid-derived aldehydes induce apoptosis: Involvement of caspases. Poster presentation at the Texas Regional Immunology Conference, November 21–23, Galveston, TX.
- Zhang, W., Khanna, P., Chan, L.N., Campbell, G. and Ansari, N.H. (1997) Diabetes-induced apoptosis in rat kidney. *Biochem. Mol. Med*. 61:58–62.

***Potential Benefits and Risks of L-Arginine Supplementation in Cancer Patients,* A Scientific Study**

In conjunction with the National Cancer Institute, the ODS is funding a project at the State University of New York Health Sciences Center at Stony Brook to study the potential benefits and risks of taking supplements of L-arginine, an amino acid, by cancer patients. Arginine influences protein synthesis rates and cell proliferation markers, and results of this study will improve understanding of how supplements of this amino acid may affect tumor stimulation and suppression. Starting date: 1997.

Publications from this study:

- Caso, G., McMillan, D.N., Eremin, O. and Garlick, P.J. Arginine and the growth of human breast tumor cells in culture. (in preparation)
- Garlick, P.J., McNurlan, M.A. and Caso, G. (1998) Critical assessment of methods used to measure protein synthesis in human subjects. *Yale J. Biol. Med.* 70:65–76.
- Garlick, P.J., McNurlan, M.A. and Caso, G. (1997) Protein turnover in cancer patients. Pp.85–101 in: *Gene Expression and Nutrition in Animals: From Cells to Whole Body*, Muramatsu, T., ed., Trivandrum, India: Research Signpost.

***Potential Role of Dietary Supplements in Reducing or Preventing Antibiotic-Induced Hearing Loss,* A Scientific Study**

The National Institute on Deafness and Other Communication Disorders and ODS are co-sponsoring a study at the University of Michigan to test the effects of dietary supplements in reducing or preventing the hearing loss that may occur with antibiotic therapy. This research may help answer questions about the relationship between nutrients and antibiotics and lead to more effective treatment strategies to prevent this form of hearing loss. Starting date: 1996.

Publications from this study:

- Sha, S-H. and Schacht, J. Mechanism and prevention of aminoglycoside-induced hearing loss. In: *Cell and Molecular Biology of the Ear*, Lim, D.J., ed., New York: Plenum Press. (in press)
- Schacht, J. Antioxidant therapy attenuates aminoglycoside-induced ototoxicity. *Ann. NY. Acad. Sci.* (in press)
- Sha, S-H. and Schacht, J. (1998) Formation of reactive oxygen species following bioactivation of gentamicin. *Free Radical Biol. Med*. 26:341-347.

- Sha, S-H. and Schacht, J. (1998) Are aminoglycoside antibiotics excitotoxic? *NeuroReport* 9:3893-3895.
- Song, B.-B., Sha, S-H. and Schacht, J. (1998) Iron chelators protect from aminoglycoside-induced cochleo- and vestibulotoxicity in guinea pig. *Free Radical Biol. Med.* 25:189–195.
- Lautermann, J. and Schacht, J. (1996) A sensitive animal model to assess acute and chronic ototoxic effects. *Arch. Otolaryngol. Head Neck Surg*. 122:837–840.
- Song, B.–B. and Schacht, J. (1996) Variable efficacy of radical scavengers and iron chelators to attenuate gentamicin ototoxicity in guinea pig *in vivo*. *Hear. Res.* 94:87–93.


***The Effect of Dietary Supplements on the Impact of Infectious Diseases on the Oral Cavity,* A Workshop**

The ODS is funding a workshop in conjunction with the National Institute of Dental and Craniofacial Research that will focus on the role of dietary supplements known to prevent or lessen oral infections. The scientific topics to be discussed will include optimal timing, dose, and potential side effects of dietary supplements related to infection. Starting date: 1999.

## PAST ACCOMPLISHMENTS

***International Workshop to Evaluate Research Needs on the Use and Safety of Medicinal Herbs,* A Workshop**

The ODS co-sponsored a workshop at the National Institute of Environmental Health Sciences (NIEHS) to identify and evaluate the major issues and key gaps in scientific research to assure the safety of medicinal herbs. Topics included the benefits and risks associated with medicinal herbs, issues of methodology and product standardization, and a panel discussion with participants from ODS, the National Center for Complementary and Alternative Medicine, the Food and Drug Administration, and other government, professional, and public interest groups. Proceedings and a summary of the workshop will be published in an upcoming issue of the NIEHS journal, *Environmental Health Perspectives.* Workshop held: September 22-23, 1998, Research Triangle Park, NC.

***Metabolic, Endocrine and Gastrointestinal Disorders in Drug Abuse and HIV/AIDS,* A Workshop**

The National Institute on Drug Abuse and the ODS co-sponsored a workshop to bring together scientists to discuss significant new research on nutrition and the immune system, specifically as they relate to disorders associated with drug abuse and HIV-infected individuals. Topics included various aspects of dietary supplements (both micronutrients and macronutrients) and their impact on the health of HIV-infected individuals, potential interventions, and recommendations for future research. The proceedings will be published in the *Journal of Acquired Immune Deficiency Syndrome* and a separate summary of this workshop will be published in the *American Journal of Clinical Nutrition.* Workshop held: August 3-4, 1998, Bethesda, MD.

***Nutritional and Health Benefits of Inulin and Oligofructose,* A Conference**

The ODS co-sponsored an international conference to review and assess current scientific evidence on the health benefits and physiological functions of inulin and oligofructose, which are fructose polymers that function in the storage of carbohydrates in plants. These compounds,

which are not digestable by humans, have properties similar to dietary fiber. Topics included the effects of inulin and oligofructose on intestinal microflora, lipid metabolism, immunity, and breast and colon cancer risk. This conference was co-sponsored with the American Dietetic Association, American Society for Clinical Nutrition, Inc., American Society for Nutrition Sciences, Canadian Society for Nutritional Sciences, Institutes of Food Technologists, ORAFTI Company, Pennsylvania State University- Department of Nutrition, and the U.S. Department of Agriculture, Agriculture Research Service. The proceedings from this workshop will be published. Workshop held: May 18-19, 1998, Bethesda, MD.

Promising New Investigator Award Recipients:

In recognition of their research efforts and to defray the cost of attendance at the conference the ODS provided support for the following scientists:

- Linda S. Boeckner, University of Nebraska
- Jennifer L. Clausey, University of Minnesota
- Kindra A. Kelly-Quaglina, Mississippi State University
- Marilynn I. Schnepf, University of Nebraska
- Steven Spector, Pennsylvania State University

***Frontiers in Antioxidant Research, ASPEN 1998,* A Workshop**

The ODS and National Institute of Diabetes and Digestive and Kidney Diseases co-funded a workshop organized by the American Society for Parenteral and Enteral Nutrition (ASPEN). The workshop brought together scientists in the field of antioxidant research to identify the most current and promising issues. Information was presented about the potential role of antioxidants in moderating human disease, including atherosclerosis and cancer. Other workshop topics included an analysis of the relationship between physical activity and oxidant exposure and research on trace nutrients that are involved in oxidant protective pathways. Workshop held: January 18, 1998 Orlando, FL.

## Goal 2: Evaluate the role of dietary supplements in physical and mental health and performance.

## ACTIVITIES IN PROGRESS:

***Coordinating Center for Clinical Trial of Hypericum perforatum (St. John's Wort) in Depressive Disorder,* A Scientific Study**

The ODS is collaborating with the National Institute of Mental Health and the National Center for Complementary and Alternative Medicine on the first large-scale, controlled clinical trial in the United States to determine the safety and efficacy of *Hypericum perforatum,* commonly known as St. John's wort, for treating patients with major depression.

This three-year trial, coordinated through Duke University Medical Center, will include 336 patients with depression as defined by the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (DSM-IV, 1994). Subjects will be randomly assigned to one of three double-blind treatments for an eight-week trial. One-third of subjects will receive a standardized daily dose (900 mg) of St. John's wort, another third will receive placebo, and the remaining will take a selective serotonin reuptake inhibitor (a medication commonly prescribed for depression). A four-month follow-up period will occur for all of the patients. Starting date: 1997.

***Bone Density Loss in Athletes,* A Scientific Study**

The ODS is co-sponsoring a study with the National Institute of Arthritis and Musculoskeletal and Skin Diseases to examine the hypothesis that inadequate calcium intake combined with substantial losses of calcium through sweat can contribute to bone loss in people participating in intensive exercise. Researchers at the University of Memphis are testing the effectiveness of calcium supplements in reducing short-term changes in bone density in male and female high school athletes. Previous studies of young, male basketball players have shown actual decreases in bone density over the course of an intense training and playing season, an observation that could have far-reaching implications for exercise in the general population. Starting date: 1996.

Publication from this study:

- Eck, L.H., Klesges, R.C., Ward, K.D., Shelton, M.L., Slawson, D.L., Cantler, E.D. and Vukadinovich, C.M. Sources of calcium intake in a sample of African-American and Euro-American collegiate athletes. *J. Nutr. Ed.* (in press).
- Kaufman, E.M. and Klesges, R.C. (1998). Does gaining weight prevent osteoporosis? An evaluation of the relationship between body fat, muscle mass, and bone density. *Ann. Behav. Med*. 20:S204.
- Peterson, B.A., Klesges, R.C., Kaufman, E.M., Cooper, T.V. and Vukadinovich, C.M. (1998). Calcium intake and bone content in young women. *Ann. Behav. Med*. 20:S213.
- Ward, K.D., Klesges, R.C., McClanahan, B., Harmon-Clayton, K., Fallone, G., Cantler, E., Palmieri, G.M.A. and Applegate, W.B. (1997). Are extremely physically active people at risk for decreases in bone mineral density? A large-scale prospective investigation. *Ann. Behav. Med*. 19:S112.
- Klesges, R.C., Ward, K.D., Palmieri, G.M.A., Applegate, W.B., Cantler, E.D. and Harmon-Clayton, K. (1996). Risk of exercise induced bone mineral loss in different team sports. *J. Bone Min. Res.* 11(suppl 1):654.

## PAST ACCOMPLISHMENTS

***Dietary Supplements for Physically Active People,* A Workshop**

The ODS initiated a major two-day workshop on the NIH campus to present a state-of-the-art scientific review of dietary supplements that may enhance the overall health of people who actively engage in exercise or recreational sports. The workshop was sponsored in conjunction with the American Institute of Nutrition and the American Society for Clinical Nutrition and was co-sponsored by eleven of the NIH ICs. The proceedings of the workshop, "The Role of Dietary Supplements for Physically Active People," were reviewed and edited by ODS and will be published as a supplement to the *American Journal of Clinical Nutrition*. A formal bibliography was prepared for this workshop in conjunction with the National Library of Medicine and is available through the *Current Bibliographies in Medicine* series. This bibliography and the scientific abstracts from this workshop are available through the ODS Internet home page (http://dietary-supplements.info.nih.gov). Workshop held: June 3-4, 1996, Bethesda, MD.

Publications from this workshop:

- Marriott, B.M. and Kanter, M., eds. (1998) The role of dietary supplements for physically active people. *Am. J. Clin. Nutr*. (in press)

- Scannell, K.M., Marriott, B.M. and Costello, R.B. (1995) *The role of dietary supplements for physically active people*: *January 1966 through April 1996*. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Library of Medicine, Reference Section, Pittsburgh, PA

On-the-Spot Award of Merit:

- Kristin Scannell, National Library of Medicine was given an On-the-Spot Award for her significant contributions to the ODS conference, "The Role of Dietary Supplements for Physically Active People," and to the development of a *Current Bibliography in Medicine* for the conference.

***The Role of Dietary Supplements in Brain Function,* A Poster Workshop**

The ODS initiated and supported the participation of speakers in a poster workshop, "Supplemental Nutrients and Brain Function" at the Sixteenth International Congress on Nutrition. This poster workshop highlighted the most recent advances relating nutrient supplementation with cognitive function and psychological disorders. Poster presenters are independently publishing their results. This session helped identify for the ODS emerging areas of supplement research related to brain function. Workshop held: July 29, 1997, Montréal, Québec, Canada.

## Goal 3: Explore the biochemical and cellular effects of dietary supplements on biological systems and their physiological impact across the life cycle.

**ACTIVITIES IN PROGRESS:**

***Modulation of Olfactory Circuits,* A Scientific Study**

The ODS is co-sponsoring with the National Institute on Deafness and Other Communicative Disorders a project at Florida State University to examine the actions of zinc and copper, two metals that are essential for proper brain development and function. The appropriate balance of these metals is strongly influenced by dietary components. Deficiencies or excesses of copper and/or zinc have been associated with a number of neuropathologic effects in humans, such as epilepsy and stroke. The primary goal of these basic research studies is to explore the modulatory actions of zinc, copper, and carnosine on several neurotransmitters (chemical messengers) expressed by olfactory bulb neurons in cultured tissue cells to focus on their role in synaptic transmission. Starting date: 1998.

***Potential Role of Dietary Tryptophan in Preventing Alcoholism in Native Americans,* A Scientific Study**

In conjunction with the National Institute on Alcohol Abuse and Alcoholism, the ODS is funding a study by Brown University investigators to examine the association between low blood levels of the amino acid, tryptophan, and increased levels of alcohol abuse and dependency in Native Americans. Low dietary intakes of tryptophan may result from a habitual diet that is high in carbohydrates and low in quality proteins. Since tryptophan is a precursor to serotonin, a neurotransmitter important in nerve function, the investigators hypothesize that Native American populations may be at risk for alcohol-related problems due to inadequate consumption of

tryptophan or one of the micronutrients that convert tryptophan to serotonin. Starting date: 1996; second award: 1998.

Publications and presentations from this study:

- Adams, W.R., Teufel, N.A., Holder, S.R., Duncan, D., Harrison, F., Miller, B.L. and Wauahdooah, B.. The tryptophan-serotonin complex and alcohol use in an Oklahoma Native American tribe. (submitted for publication)
- Adams, W.R., Holder, S.R., Teufel, N.A., Duncan, D., Harrison, F., Miller, B.L. and Wauahdooah, B. (1998) The impact of tryptophan, vitamin B6, ascorbic acid, and zinc intake on alcohol use in an Oklahoma Native American tribe." Alcohol and Drug Study Group Bulletin 34(1):10-13.
- Duncan, D., Adams, W.R., Holder, S.R., and Teufel, N.A. (1998) Diet and alcohol consumption in an Oklahoma Native American population. Presentation at the Nutrition and Public Health Ninety-seventh Annual Meeting of the American Anthropological Association, December 2-6, 1998, Philadelphia, PA.

***Potential Benefits of Intestinal Amino Acid Supplementation in Infants with Ineffective Intestinal Metabolic Function,* A Scientific Study**

The ODS and the National Institute of Child Health and Human Development (NICHD) are co-sponsoring a project at Baylor College of Medicine in Houston, Texas, to measure the benefits of intestinal supplementation of three amino acids—glutamate, glycine, and cysteine—in infants with ineffective intestinal metabolic function. The study will help clarify the role of these key amino acids in the inhibition and stimulation of glutathione synthesis in the intestinal tract. Glutathione is a substance that may have a protective role against dietary and bacterial toxins. Starting date: 1997.

Publications and presentations from this study:

- Reeds, P.J., Burrin, D.G., Stoll, B. and Jahoor, F. Intestinal glutamate metabolism. *J. Nutr*. (in press)
- Stoll, B., Burrin, D.G., Henry, J., Yu, H., Jahoor, F. and Reeds, P.J. Substrate oxidation by the portal drained viscera of fed piglets. *Am. J. Physiol.* (in press)
- Reeds, P.J. (1998) Intestinal glutamate metabolism. Presentation at the International Glutamate Symposium, October 11-15, 1998, Bergamo, Italy.

***Brain MR Spectroscopic Studies of Thiamin Deficiency; Effect of Thiamine Deficiency and Its Treatment on Brain Neurochemical Markers,* A Scientific Study**

The ODS is co-funding a study with the National Institute of Neurological Disorders and Stroke to examine thiamin deficiency and its treatment on brain neurochemical markers. This study uses magnetic resonance imaging techniques to carefully examine the effects of thiamin treatment alone and in combination with a number of neuroprotective agents. Thiamine deficiency, a frequent complication of alcoholism, can result in brain damage and severe deficits in cognitive function if left untreated. The results of this study will enhance understanding of (1) neurobiological consequences of alcohol and metabolically induced thiamin deficiency related to brain damage, (2) its treatment, and (3) prevention. Starting date: 1996.

***Zinc and Health: Current Status and Future Directions,* A Workshop**
***Zinc: What Role Might Supplements Play?* A Conference**

The ODS initiated a two-day workshop, followed by a one-day conference, to provide an overview of the biochemical, cellular, and nutritional requirements of zinc in health and disease and the role of dietary supplementation with zinc. The meetings were co-sponsored by six NIH institutes and offices, other federal agencies, and two professional associations. Attention was focused on the key areas where zinc supplementation may play a role in the prevention, reduction or treatment of disease. These meetings brought together leading experts in zinc research and clinicians from many scientific disciplines to present a timely update and critical needs assessment on zinc and health to researchers, nutritionists, public health advisers, and policy makers. These scientists presented reviews of the current state of scientific knowledge that are applicable to many basic science, clinical, and public health programs across the country. The workshop sessions focused on: zinc and the immune system, gastrointestinal tract, and the central nervous system; antioxidant and defense functions of zinc; zinc and cellular mechanisms; and zinc in growth and specific disease entities. New and emerging roles of zinc and zinc supplementation in human health were also discussed, as well as new measurement and assessment techniques that are available in the field of zinc research. Key areas that warrant further investigation were also identified. The one-day conference was focused on the question of zinc supplementation and summarized for the public the relevant findings on dietary zinc requirements, the regulation of zinc metabolism, zinc and development, zinc and immune function, zinc metabolism in disease, and zinc intake of the U.S. population.

The ODS will publish the proceedings of the workshop as a supplement to the *Journal of Nutrition*. A formal bibliography was prepared in conjunction with the National Library of Medicine and is available through the *Current Bibliographies in Medicine* series. This bibliography and the scientific abstracts from the conference are available through the ODS Internet home page (http://dietary-supplements.info.nih.gov). Workshop held: November 4-5, 1998, Bethesda, MD. Conference held: November 6, 1998, Bethesda, MD.

Publications from this workshop:

- Glazer, A., Scannell, K.M., Costello, R.B., Krakower, T.J. and Marriott, B.M., compilers.(1998) *Zinc and health* [bibliography on the Internet]. Bethesda, MD: National Library of Medicine, 1998 Oct. (Current bibliographies in medicine, no. 98-3). 3619 citations from January 1990 through June 1998. Available from http://www.nlm.nih.gov/pubs/resources.html.

## PAST ACCOMPLISHMENTS

***Establishing Upper Safe Limits for B Vitamin Intake,* A Scientific Report**

The ODS co-funded with the Centers for Disease Control and Prevention and the Food and Drug Administration an 18-month National Academy of Sciences project on the Dietary Reference Intakes (DRIs) (formerly called the Recommended Dietary Allowances) for folate and other B vitamins. The ODS specifically funded a contract to the Food and Nutrition Board (FNB), Institute of Medicine, to continue and extend their consideration of DRIs for folate and related nutrients to include the development of Tolerable Upper Intake Levels (ULs) of safety. The FNB has established a Subcommittee (within the Standing Committee on the Scientific Evaluation of DRIs) on the Upper Safe Reference Levels of Nutrients. This subcommittee developed a risk assessment model to establish maximum levels of nutrient intakes that are

compatible with low risk of toxicity. Through this project, the subcommittee applied the model to scientific information on folate and related nutrients. As part of the process, the FNB held workshops to solicit the opinions of experts and practitioners in conjunction with a public forum. The final report, *Dietary reference intakes for thiamin, riboflavin, niacin, vitamin $B_6$, folate, vitamin $B_{12}$, pantothenic acid, biotin, and choline* (IOM, 1998) establishes maximum levels of intake compatible with low risk of toxicity and, where adequate information is available, provides recommendations for upper levels of safety for folate, vitamin $B_{12}$, vitamin $B_6$, and related nutrients. The full report is available from the National Academy Press or through the FNB web site (http://www2.nas.edu/fnb/). Report released: 1998.

Scientific report:

- Institute of Medicine (IOM) (1998) *Dietary reference intakes for thiamin, riboflavin, niacin, vitamin $B_6$, folate, vitamin $B_{12}$, pantothenic acid, biotin, and choline.* National Academy of Sciences, Food and Nutrition Board. Washington, D.C.: National Academy Press.

***Role for Coenzyme $Q_{10}$ in the Aging Process: Potential Benefits of $Q_{10}$* Supplementation, A Workshop**

The ODS co-funded a workshop organized by the National Institute on Aging on the role of coenzyme $Q_{10}$ and the aging process. Discussions focused on the role of coenzyme $Q_{10}$ as a synergistic antioxidant, the regulatory role of coenzyme $Q_{10}$ by nitric oxide in the mitochondria, and the long-term effects of coenzyme $Q_{10}$ supplementation. New data and insight provided a possible role of coenzyme $Q_{10}$ in neurodegenerative diseases such as Parkinson's and Huntington's diseases and in cardiovascular diseases. However, the group concurred that much is still to be learned about basic biochemical pathways and metabolism and bioavailability of coenzyme $Q_{10}$. Workshop held: August 31–September 1, 1998, Bethesda, MD.

***Genetic and Environmental Determinants of Copper Needs Across the Life Span,* A Workshop**

The ODS co-sponsored a workshop initiated by the Fogarty International Center and the University of Chile; other co-sponsors included the National Institutes of Child Health and Human Development, National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Environmental Health Sciences, and the Environmental Protection Agency. The workshop brought together over 60 international scientists from academia, industry, and government agencies that work in the area of copper metabolism, requirements, or toxicity. This group reviewed, from an international perspective, the recent significant advances in understanding of the molecular mechanisms underlying genetic disorders of copper metabolism and their implications for copper intake and exposure. One session of the workshop focused on the difficult question of how to adequately measure copper status in humans. The conference further identified research gaps related to copper requirements, copper-nutrient interactions, and specific disease end points with regard to dietary supplementation with copper. Workshop held: March 18–20, 1996, Bethesda, MD.

Publication from this workshop:

- Lönnerdal, B. and Uauy, R., eds. (1998) Genetic and environmental determinants of copper metabolism. Proceedings of an international conference held in Bethesda, MD, March 18–20, 1996. *Am. J. Clin. Nutr*. 67:5(S).

***Essential Fatty Acids in the Treatment of Mental Disorders,* A Workshop**

A recent workshop on essential omega-3 fatty acids and psychiatric disorders was organized by National Institute on Alcohol Abuse and Alcoholism and the National Institute of Mental Health and co-sponsored by the ODS and the Office of Research on Women's Health. This workshop brought together international scholars to discuss new areas of research on omega-3 polyunsaturated fatty acids, with a focus on metabolic and clinical studies related to psychiatric disorders. The proceedings and a summary of this workshop will be published. Workshop held: September 2–3, 1998, Bethesda, MD.

***Phospholipids in Health and Disease,* A Conference**

The ODS Director cochaired a session at the Seventh International Congress on Phospholipids in Brussels, Belgium. The meeting focused on choline and choline phospholipids and included the following topics: cell signaling, cell suicide pathways, phosphatidylcholine biosynthesis, and various issues related to choline and health. Of particular interest to the ODS were the sessions on choline and brain function. Animal model studies have shown consistent results in choline-induced memory improvements in young as well as aged animals. Sex differences were observed with perinatal treatment that demonstrated long-lasting improvement in memory capacity in male animals, but the effects were of smaller magnitude and shorter duration in female animals. These data, coupled with the basic science studies, presented a well-rounded overview of the recent findings in phospholipid research and identified areas for future study of importance to the ODS. Conference held: September 8–10, 1996, Brussels, Belgium.

***Approach to the Prevention of Orofacial Clefts,* A Workshop**

The director of ODS participated in a workshop, "Approach to the Prevention of Orofacial Cleft," with the Director, National Institute of Dental and Craniofacial Research. The workshop was co-sponsored by the March of Dimes Foundation, California Birth Defects Monitoring Program, and the Centers for Disease Control and Prevention to evaluate recent research findings and discuss future research possibilities. This first meeting focused on the potential role for ingestion of periconceptual folic acid supplements to reduce the risk of cleft lip with or without cleft palate. Additional meetings are planned to further review the literature and plan possible joint activities. Workshop held: March 17–18, 1996, Emeryville, CA.

***Melatonin and Aging,* A Workshop**

The ODS co-sponsored a workshop initiated by the National Institute on Aging to assess the current status of research on melatonin and aging and to recommend future research opportunities. Topics discussed included the effects of melatonin on the processes of aging and on the circadian clock system, as well as age-related changes in melatonin levels. Workshop held: August 14–16, 1996, Berkeley, CA.

***Melatonin and Sleep,* A Workshop**

A workshop on melatonin and sleep was initiated by the National Institute on Aging and co-sponsored by the ODS. Research studies that focus on the biochemistry, pharmacology, and neuroendocrinology of melatonin and its effects on various sleep parameters were presented. Research areas that need further study were also identified. Workshop held: August 12–13, 1996, Bethesda, MD.

Publication from this workshop:

- Lamberg, L. (1996) Melatonin potentially useful but safety, efficacy remain uncertain. *J. Am. Med. Assoc*. 276(13):1011–1014.

**Goal 4: To advance scientific methodology, including epidemiology, in the characterization of dietary supplements.**

**ACTIVITIES IN PROGRESS:**

***Zinc Kinetics in Metallothionein Knockout Mice,* A Scientific Study**

In conjunction with the National Institute of Diabetes and Digestive and Kidney Diseases, the ODS is funding a project at Georgetown University, Department of Pediatrics, in which the investigators are studying the role and action of a key zinc regulatory enzyme, metallothionein, on the distribution, metabolism, and homeostasis of zinc. This research team will use kinetic studies with radioactive tracers in knockout animals (animals devoid of the metallothionein enzyme) to determine zinc absorption and tissue distribution in a mouse model. This research offers insight into the role of specific gene product(s) on nutrition and metabolism. Starting date: 1998.

***Mechanisms of Antifolate Efficacy in Arthritis,* A Scientific Study**

The ODS is co-funding a study with the National Institute of Arthritis and Musculoskeletal and Skin Diseases that is being conducted by researchers at the University of Alabama at Birmingham. The project examines the interactions between methotrexate treatment for rheumatoid arthritis and both dietary folic and folinic acid in rats. Results of this study may help identify one or more biochemical pathways related to folate metabolism that are critical for the induction of inflammation and tissue injury in arthritis. It could also contribute to the development of more specific drugs to control arthritis that interfere minimally with the reduction of dietary folic acid and the recycling of intracellular dihydrofolates. Starting date: 1996.

Publications from this study:

- Baggott, J.E., Morgan, S.L., Sams, W.M. and Linden, J. Urinary adenosine and aminoimidazolecarboxamide excretion in methotrexate-treated psoriasis patients. (submitted for publication)
- Baggott, J.E., Morgan, S.L. and Koopman, W.J. (1998) The effect of methotrexate and 7-OH methotrexate on rat adjuvant arthritis and on urinary aminoimidazole carboxamide excretion. *Arthritis Rheum.* 41:1407–1410.
- Morgan, S.L., Baggott, J.E., Lee, J.Y. and Alarcon, G.S. (1998) Folic acid supplementation prevents deficient blood folate levels and hyperhomocysteinemia during long-term, low dose methotrexate therapy for rheumatoid arthritis: Implications for cardiovascular disease prevention. *J. Rheumatol.* 25: 441–446.
- Morgan, S.L. and Weinsier, R.L., eds. (1998) *Fundamentals of clinical nutrition,* 2d ed. St. Louis, MO.: Mosby.
- Tamura, T., Bergman, S.M. and Morgan, S.L. (1998) Hyperhomocysteinemia as a cause of vascular thrombosis in patients with end-stage-renal disease. *Int. J. Artif. Organs* 21:72–74.

- Morgan, S.L., Baggott, J.E. and Alarcon, G.S. (1997) Methotrexate in rheumatoid arthritis. Folate supplementation should always be given. *BioDrugs* 8(3):164–175.
- Morgan, S.L., Baggott, J.E., Lee J.Y. and Alarcon, G.S. (1997) Folic acid prevents elevated homocysteine (hcy) levels during methotrexate (MTX) therapy. *Arthritis Rheum.* 40:S53.

***Vanadium Salts and Carbohydrate Metabolism,* A Scientific Study**

The ODS and the National Institute of Diabetes and Digestive and Kidney Diseases are co-sponsoring a project at the Albert Einstein College of Medicine to study dose-response patterns of vanadium, a trace element found in a number of spices and health food supplements. Vanadium has been shown to mimic the action of insulin and has been used to treat hyperglycemia in animals with diabetes. This study will obtain dose-response data in order to assess the toxicity and safety of vanadium use in humans. Starting date: 1996.

Publications from this study:

- Aharon, Y., Mevorach, M., Rossetti, L. and Shamoon, H. (1998) Vanadyl sulfate does not enhance insulin action in patients with type I diabetes. *Diabetes Care* 21:2194-2195.
- Aharon, Y., Mevorach, M. and Shamoon, H. (1997) Vanadyl sulfate does not enhance insulin action in patients with IDDM. *Diabetes* 46(suppl 2):95A.
- Cohen, N., Halberstam, M., Shlimovich, P., Chang, C.J., Rossetti, L. and Shamoon, H. (1996) Oral vanadyl sulfate improves hepatic and peripheral insulin sensitivity in NIDDM but not in obese nondiabetic subjects. *Diabetes* 45:659–66.

**PAST ACCOMPLISHMENTS:**

***Lutein and Zeaxanthin: Safety and Procedural Issues for Supplementation in Relation to the Development of Macular Degeneration,* A Workshop**

The ODS co-sponsored a workshop initiated by the National Eye Institute that focused on two carotenoids, lutein and zeaxanthin, that have a potential role in preventing and treating eye diseases. Some of the topics that were evaluated were expected mechanisms of action, safe dosage levels, and potential interactions with vitamins, minerals, and drugs. A major goal of the workshop was to identify new directions for research. Workshop held: February 10, 1998, Bethesda, MD.

**Goal 5: Inform and educate scientists, health care providers and the public about the benefits and risks of dietary supplements.**

**ACTIVITIES IN PROGRESS:**

***International Bibliographic Information on Dietary Supplements (IBIDS),* A Database**

The ODS completed a database to address the DSHEA mandate to "collect and compile the results of scientific research relating to dietary supplements." The purpose of the International Bibliographic Information on Dietary Supplements (IBIDS) is to assist both researchers and the general public in locating scientific literature on dietary supplements. IBIDS contains published, international, scientific literature on dietary supplements from multiple medical and scientific databases from 1985 to the present. Monographs, serials, reports, and literature from the previous decade will be added to IBIDS during a second phase of

development. IBIDS is accessible to the public on the ODS World Wide Web home page (http://dietary-supplements.info.nih.gov) through a user-friendly search engine. The search engine was designed to accommodate all levels of expertise and includes easy-to-use, drop-down menus with standard dietary supplements terminology, as well as more complex Boolean search methods.

IBIDS was developed through an interagency cooperative agreement between the ODS and the Food and Nutrition Information Center, National Agricultural Library, Agricultural Research Service, U.S. Department of Agriculture. The IBIDS team developed, tested, and optimized a novel search strategy that was necessary because the databases use different formats and key words. IBIDS will be updated quarterly and evaluated periodically to ensure that the appropriate journals are being reviewed, that the search strategy is current, and that it continues be cost effective. Starting date 1996, completion: January, 1999.

***Computer Access to Research on Dietary Supplements (CARDS),* A Database**

DSHEA also mandated that the ODS "compile a database of scientific research on dietary supplements and individual nutrients." The ODS is currently developing this second database, Computer Access to Research on Dietary Supplements (CARDS). CARDS is designed to provide information about research on dietary supplements and individual nutrients that is currently supported by the federal government. CARDS will be, in part, a derivative database from the new NIH information system, IMPAC II. CARDS will be available through the ODS Internet home page (http://dietary-supplements.info.nih.gov) and will be accessed through a user-friendly search engine designed for all levels of expertise. The ODS is developing a monitoring system to ensure that CARDS continues to be accurate and timely and that it operates cost effectively. Starting date: 1996, completion expected: 1999.

***Information Center Needs Assessment Study,* A Scientific Study**

The ODS contracted with the Human Nutrition Information Center (FNIC), National Agricultural Library, U.S. Department of Agriculture, to conduct a formal study to determine the need for a Dietary Supplements Information Center. Although DSHEA did not mandate that the ODS provide a public information center on dietary supplements, the ODS continues to receive numerous requests for information on specific supplements from scientists, policy makers, patients, clinicians, and concerned citizens via telephone, letters, E-mail, and in person. These inquiries reflect the public's keen interest in issues related to dietary supplements, health, and performance. During its first year as a small, new office, the ODS attempted to respond to all inquiries, but it did not have the resources to address the volume or diversity of public inquiries related to dietary supplements. Currently, the ODS refers information requests to the FNIC. This study will result in a detailed, published report that quantifies the volume and diversity of public inquiries related to dietary supplements and specifies how these inquiries are being met. A key outcome of the study will be an assessment of the need for a federally-funded public information center on dietary supplements. Report expected: 1999.

***Dietary Supplement Fact Sheets,* An Information Source**

The ODS is collaborating with the NIH Warren Grant Magnuson Clinical Center to produce peer-reviewed fact sheets about selected vitamins, minerals, and botanicals in order to inform and educate the public, health care providers, and scientists about the benefits and risks associated with these dietary supplements. The nutrient fact sheets will summarize current

scientific information on what each nutrient is, what foods provide it, who is most likely to develop a deficiency, who should be cautious about taking the supplement, and potential interactions. The botanical supplements will follow a parallel format. The fact sheets will be installed on the ODS World Wide Web home page (http://dietary-supplements.info.nih.gov) as they become available and upon request. Starting date: 1998.

***CD-ROM Dietary Supplement Educational Module,* An Information Source**

To improve medical school education about the benefits and risks of dietary supplements in health care, the ODS is collaborating with the developers of a CD-ROM educational program, *Nutrition in Medicine*, which has been successfully introduced into medical school curricula. The ODS is supporting a dietary supplement module for this series. Starting date:1998.

**PAST ACCOMPLISHMENTS:**

***World Wide Web Home Page,* An Information Source**

The ODS recently completed an Internet home page (http://dietary-supplements.info.nih.gov) to disseminate information as broadly as possible. The web site provides information about the ODS, including its origins, mandates, mission statement, and strategic plan. It also will provide public access to the ODS scientific databases on dietary supplements research (IBIDS and CARDS); ODS publications; grant, funding, and partnering opportunities that are currently sponsored by NIH; and other activities and scientific resources. The ODS web site will be a dynamic, evolving project that will be enhanced and updated as information becomes available, as the needs of users change, or as new discoveries about dietary supplements are revealed through the research. Starting date: July 1998.

<u>On-the-Spot Award of Merit:</u>

- William Hall, Director of Communications, Office of Medical Applications of Research, Office of the Director, NIH, received an On-the-Spot Award of Merit in July 1998 for his outstanding contribution to the development of the ODS Internet home page.

***The Problem of Overcoming Selenium Deficiency in the Russian Federation,* A Workshop**

This workshop's purpose was to exchange recent research findings on selenium deficiency and supplementation; to obtain detailed information on selenium status in the Russian Federation; and to discuss various countries' intervention approaches in alleviating selenium deficiencies, including supplementation with selenium of high bioavailability (such as fortified yeast). A secondary objective was to bring together current research findings on the role of selenium in cancer prevention.

The workshop built on joint activity in the area of micronutrient malnutrition, begun under the auspices of the Health Committee of the U.S.–Russia Commission on Economic and Technological Cooperation. On the U.S. side, major support was provided by the ODS, National Cancer Institute, the National Institute of Diabetes and Digestive and Kidney Diseases, and the U.S. Agency for International Development.

U.S. and international participants included government and academic representatives from the United States, China, Finland, and New Zealand. The U.S. government representation included the U.S. Department of Health and Human Services and the U.S. Department of Agriculture . The Russian representation included the Institute of Nutrition, as well as the Research Center for Preventive and Therapeutic Nutrition of the Russian Academy of Medical

Sciences and its Siberian Division. Workshop held: June 16–19, 1998, Moscow and Tyumen, Russia.

***The Path to Maternal and Child Health: The PVO Role in Improving Iron and Vitamin A Status,* A Workshop**

An international workshop was organized by the Child Survival Collaborations and Resources Group, a consortium of private, voluntary organizations (PVOs), supported by the U.S. Agency for International Development and working in child survival issues. Representatives from 80 organizations attended, including managers of micronutrient programs in Africa, Southeast Asia, Latin America, and Russia. The ODS supported the participation of six Russian PVO program managers and clinicians in the workshop to build on U.S.–Russian collaboration in the area of micronutrient malnutrition. This effort calls for multiagency, multidisciplinary cooperation to identify more precisely the nutritional status of the U.S. and Russian populations; to focus on areas where more research is needed; to develop and implement appropriate and sustainable interventions; and to perform regular surveillance to assess the effectiveness, safety, and quality of such interventions. The workshop served as a forum to exchange current knowledge on the epidemiological profile of iron deficiency and intervention practices in the Russian Federation and to further define plans for joint activities in order to alleviate this serious deficiency. Workshop held: May 5–7, 1998, Washington, DC.

# BUDGET

At its inception, the ODS was authorized to receive $5 million. “AUTHORIZATION OF APPROPRIATIONS.- There are authorized to be appropriated to carry out this section $5,000,000 for fiscal year 1994 and such sums as may be necessary for each subsequent fiscal year.” (Public Law 103-417, Section 13. [a]). This amount was not appropriated, however, and the Director, NIH funded the ODS start-up costs for 1995 through the NIH Director’s Discretionary Fund. Since fiscal year (FY) 1996, the operating and program funds for the ODS have been funded as a line item in the Office of the Director’s budget. The operating levels for FY 1996 through 1999 increased (dollars in thousands): FY 1996, 999; FY 1997, 997; FY 1998, $ 1,497; FY 1999, $ 3,504. The focus of ODS expenditures has been promotion and support of research and fulfilling the tasks mandated by Congress.

# CONCLUSION AND A LOOK TO THE FUTURE

This report summarizes the activities and accomplishments of the ODS during its initial years, from 1995 to 1998. Collectively, the activities aim to fulfill the Congressionally mandated purpose of the office, to promote the scientific study of the benefits and risks of dietary supplements in health maintenance and disease prevention. The major areas of emphasis are to provide the stimulus, training, and support for research and to disseminate research results in order to increase the scientific base of the field of dietary supplements. A solid scientific base is necessary for informed and safe decision making by the public and by government agencies responsible for health policy.

The ODS has forged collaborations among the NIH ICs, other government agencies, and academic institutions to fund dietary supplement ingredient research. Some of the research projects currently supported by the ODS focus on aspects of many of the major diseases, such as cardiovascular disease, arthritis, alcoholism, clinical depression, oral and eye disease; other studies focus specifically on patients with diabetes and cancer. Additional research funded by the ODS focuses on issues such as dietary supplement safety and supplement use by athletes involved in intensive exercise programs.

In addition to funding research, the ODS has been developing tools and resources for use by the research community. Two dietary supplement research databases that were Congressionally mandated have moved into their final phases of development. The first database (IBIDS) is a collection of current, peer-reviewed scientific literature on dietary supplements. The second (CARDS) is a compilation of federally funded research on dietary supplements. Both databases will be available through the ODS web site on the Internet and have user-friendly search engines to accommodate various levels of expertise.

The ODS has initiated or co-funded numerous workshops and conferences (see Appendix D) to bring together scientists who are working in a specific area, to facilitate exchange of the most current information, and to define research gaps that need further study. Proceedings and summaries of these conferences have been published in scientific journals in order to disseminate research findings to the scientific community.

The future direction of the ODS will be guided by its recently completed strategic plan, *Merging Quality Science with Supplement Research, A Strategic Plan for the Office of Dietary Supplements* (ODS, 1998) (see Appendix B for executive summary). In it, the ODS established five key scientific goals and objectives that will be emphasized in new and continuing activities.

The ODS will continue to support investigator-initiated research through the Research Enhancement Awards Program (REAP) and joint program announcements with the NIH ICs and to stimulate further research by conducting conferences, workshops, and presentations at national and international meetings.

The ODS believes that there is a need to establish Centers for Dietary Supplement Research to effectively promote dietary supplement research. A research center is a group of collaborating scientists who conduct research on a common problem and often share resources and facilities (see Types of Activities). The ODS seeks to collaborate with the NIH ICs, other government agencies, and industry to jointly develop and fund research centers that will focus on the efficacy and safety of dietary supplements and on basic scientific issues of characterization and quality. These centers will be developed following standard NIH competitive centers mechanisms and, where possible, will build on the infrastructure of existing government-funded research centers to reduce overhead costs and maximize money directed toward research. It is

expected that some or all of these centers will be linked as consortia in order to share expertise, resources, and facilities and to avoid duplication.

To educate the public about specific dietary supplement issues, the ODS is jointly developing with the Warren Grant Magnuson Clinical Center, NIH, a set of public-oriented fact sheets about specific dietary supplements that will be available on request and through the Internet. These fact sheets, which will be peer-reviewed, will present and interpret the scientific literature in a more applied sense. The ODS is also collaborating with the developers of a CD-ROM educational program to support a dietary supplement module for medical student education.

The ODS looks forward to continuing its efforts to fulfill the mandates set forth for it by Congress, that is "to promote the scientific study of dietary supplements for maintaining health and preventing chronic diseases and other health-related conditions" (DSHEA, 1994) for the American people.

# REFERENCES


Aarts, T., ed. (1998) Nutrition industry overview. *Nutr. Bus. J.* 3(9):1-5.

DHHS (U.S. Department of Health and Human Services) (1997) Strategic plan.

DSM- IV (*Diagnostic and statistical manual of mental disorders*, fourth ed.) (1994) Task Force on DSM-IV and Other Committee and Work Groups of the American Psychiatric Association. Washington, D.C.: American Psychiatric Association.

IOM (Institute of Medicine) (1998) *Dietary reference intakes for thiamin, riboflavin, niacin, vitamin $B_6$, folate, vitamin $B_{12}$, pantothenic acid, biotin, and choline.* A report of the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes and its Panel on Folate, Other B Vitamins, and Choline and Subcommittee on Upper Reference Levels of Nutrients, Food and Nutrition Board. Washington, D.C.: National Academy Press.

Lewis, K.A. and Hohl, R.J. (1997) Modulation of RAS expression in human malignant cells by dietary supplements. *Nutrition* 13(10):921-923.

NIH (National Institutes of Health) (1997) Setting research priorities at the National Institutes of Health, NIH Working Group on Priority Setting. NIH Publication No. 97-4265. Bethesda, MD.

ODS (Office of Dietary Supplements) (1998) Merging quality science with supplement research, A strategic plan for the Office of Dietary Supplements. NIH Publication No. 99-4356.

Public Law 103-417, 103d Congress, 2d session. (25 October 1994) Dietary Supplement Health and Education Act of 1994.

Slesinski, M.J., Subar, A.F. and Kahle, L.L. (1995) Trends in use of vitamin and mineral supplements in the United States: The 1987 and 1992 National Health Interview Surveys. *J. Am. Diet. Assoc.* 95:921-923.

# APPENDIXES

## Appendix A
## Excerpt from the Dietary Supplement Health and Education Act of 1994

The Dietary Supplement Health and Education Act (DSHEA) (Public Law 103-417, Section 13.[a]) set out the following functions and duties for the Office of Dietary Supplements (ODS) as authorized at the National Institutes of Health:

**"SEC. 485C. DIETARY SUPPLEMENTS.**

"(a) ESTABLISHMENT.-The Secretary shall establish an Office of Dietary Supplements within the National Institutes of Health.

"(b) PURPOSE.-The purposes of the Office are--

"(1) 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; and

"(2) to promote scientific study of the benefits of dietary supplements in maintaining health and preventing chronic disease and other health-related conditions.

"(c) DUTIES.-The Director of the Office of Dietary Supplements shall—

"(1) conduct and coordinate scientific research within the National Institutes of Health relating to dietary supplements and the extent to which the use of dietary supplements can limit or reduce the risk of diseases such as heart disease, cancer, birth defects, osteoporosis, cataracts, or prostatism;

"(2) collect and compile the results of scientific research relating to dietary supplements, including scientific data from foreign sources or the Office of Alternative Medicine;

"(3) serve as the principal advisor to the Secretary and to the Assistant Secretary for Health and provide advice to the Director of the National Institutes of Health, the Director of the Centers for Disease Control and Prevention, and the Commissioner of Food and Drugs on issues relating to dietary supplements including--

"(A) dietary intake regulations;

"(B) the safety of dietary supplements;

"(C) claims characterizing the relationship between--

"(i) dietary supplements; and

"(ii)(I) prevention of disease or other health-related conditions; and

"(II) maintenance of health; and

"(D) scientific issues arising in connection with the labeling and composition of dietary supplements;

"(4) compile a database of scientific research on dietary supplements and individual nutrients; and

"(5) coordinate funding relating to dietary supplements for the National Institutes of Health."

# Appendix B
# Strategic Plan Executive Summary

## Merging Quality Science With Supplement Research: A Strategic Plan For The Office Of Dietary Supplements

The Office of Dietary Supplements (ODS) was established by the Dietary Supplement Health and Education Act of 1994 (DSHEA, Public Law 103-417) that amended the Federal Food, Drug, and Cosmetic Act "to establish standards with respect to dietary supplements." The ODS was placed at the National Institutes of Health (NIH) in the Office of the Director. Formal operations began in November 1995.

*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.*

**The purposes of the ODS within the NIH are:**

- ". . . 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; and
- . . . to promote the scientific study of the benefits of dietary supplements in maintaining health and preventing chronic disease and other health-related conditions."

**The duties of the ODS are to:**

- "conduct and coordinate scientific research within the National Institutes of Health relating to dietary supplements and the extent to which the use of dietary supplements can limit or reduce the risk of diseases such as heart disease, cancer, birth defects, osteoporosis, cataracts, or prostatism;
- collect and compile the results of scientific research relating to dietary supplements, including data from foreign sources or the Office of Alternative Medicine;
- serve as the principal advisor to the Secretary and to the Assistant Secretary for Health and provide advice to the Director of the National Institutes of Health, the Director of the Centers for Disease Control and Prevention, and the Commissioner of Food and Drugs on issues relating to dietary supplements;
- . . . compile a database of scientific research on dietary supplements and individual nutrients; and
- coordinate funding relating to dietary supplements for the National Institutes of Health." (DSHEA, 1994)

**Goals and Objectives:**

The ODS has identified the following five equally weighted goals and related objectives that will guide ODS activities on an annual basis:

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

Over 100 million Americans regularly use dietary supplements. Many supplement users report that they take dietary supplements to reduce the risk of disease or generally to promote health. Disease prevention research includes the identification of risk factors and interventions that prevent the occurrence of disease (or its progression, if detectable but asymptomatic). In a broader sense, it also includes analysis of the etiology and mechanisms of disease that may contribute basic knowledge applicable to future preventive interventions. As a unit within the NIH, the ODS must promote and support basic research that is likely to advance particular areas of science that may be relevant to clinical studies of efficacy and safety and specific health problems.

To address Goal 1, the ODS sets the following objectives:

- Advance the understanding of the specific impact of nutrient and botanical supplements or their ingredients on immunocompetence particularly related to HIV/AIDS and infectious agents.
- Stimulate research on the potential roles of dietary supplements in reducing the risk and control of cancer,[*] particularly cancer of the breast, ovary, and prostate.*
- Evaluate the role of specific supplements in reducing the symptoms or pathology of coronary heart disease* and diabetes.
- Identify those dietary supplements that reduce the symptoms of, and possibly retard the progression of arthritis, including osteoarthritis.
- Introduce a cross-disciplinary initiative to study the interactions among diet, supplements, and physical activity in bone health and reducing the risk and progression of osteoporosis.*
- Develop strategies to evaluate the role of individual and multiple supplements to reduce the risk and progression of ocular disease, particularly cataracts* and macular degeneration.
- Foster the inclusion of research on the role of dietary supplements in federal initiatives to address the etiology, reduction, and health outcomes of obesity in the U.S. population.
- Examine whether dietary supplement use may influence the progression of oral diseases.

**Goal 2: Evaluate the role of dietary supplements in physical and mental health and in performance.**

In 1996, the U.S. Surgeon General issued a report recommending that Americans increase their physical activity. In response to the Senate Appropriations Committee of the U.S. Congress, the Institute of Medicine, National Academy of Sciences prepared a report that detailed recommendations for mental health research. In keeping with these reports and the congressional mandate, ODS seeks to promote research on the scientific benefits and risks of dietary supplements in maintaining health and performance.

[*] Specific areas of scientific priority included in the DSHEA legislation.

The following are objectives to address Goal 2:

- Encourage research efforts to evaluate the relationships among dietary supplements and physical health and performance that includes the full range of age and population groups, hydration status, temperature regulation, environmental stress, and physical activity.
- Advance research on the role of dietary supplements in altering body composition and weight control.
- Advance research on the role of dietary supplements for increasing muscle strength, endurance, conditioning, and anaerobic power.
- Initiate research to identify and characterize the unique nutrient and caloric needs of persons with disabilities and elucidate potential roles for dietary supplements.
- Encourage research to determine the beneficial and detrimental effects of dietary supplements on mood, fatigue, stress, and psychological well-being.
- Promote further study of dietary supplements that have been demonstrated scientifically to enhance cognitive performance.

**Goal 3: Explore the biochemical and cellular effects of dietary supplements on biological systems and their physiological impact across the life cycle.**

The use of dietary supplements may influence biological systems or the physiological challenges to these systems during human development. One function of the ODS is to define areas of research focus and foster exploration of the biologic variables related to acute and chronic use of dietary supplements.

The following objectives have been identified to carry out this goal:

- Investigate how dietary supplements may moderate specific processes of aging.
- Explore how the assimilation of dietary supplements varies with age-related physiologic changes.
- Advance the understanding of how dietary supplements may influence reproductive systems, birth defects,[*] and fetal development.
- Characterize the relationships among dietary supplements and basic cognitive processes, including attention, learning, and memory.
- Evaluate the role of individual supplements and supplement ingredients in the underlying pathophysiology of metabolic, endocrine, and gastrointestinal disorders, particularly those associated with drug and alcohol abuse.
- Identify the changes in basic metabolic and physiologic processes that may occur with physical disabilities and potential roles for dietary supplements.

**Goal 4: Improve scientific methodology as related to the study of dietary supplements.**

Dietary supplement research is conducted across many scientific disciplines and supported by a wide array of methods. Key to enhancing progress in the field is the integration of research that accommodates the variety of supplements, supplement delivery systems, sites and mechanisms of action, and groups of individuals who take supplements. Scientific

[*] Specific areas of scientific priority included in the DSHEA legislation.

advancement with a particular supplement may hinge, therefore, on the development or refinement of appropriate and/or novel instrumentation or methods.

To meet this goal, the ODS proposes the following objectives:

- Promote the identification and characterization of bioactive compounds in dietary supplements by delineating their mode of absorption, distribution, metabolism, mechanism of action, and excretion.
- Evaluate and develop animal and clinical methods for determining the efficacy and safety of dietary supplements.
- Develop new and validate existing epidemiological/survey methods for assessing dietary supplement usage.
- Promote the collection of reliable and valid data on dietary supplement usage.
- Promote academic-government-industry partnerships to advance dietary supplement research and technology transfer.
- Develop model systems to predict and characterize the potential for adverse effects resulting from interactions among dietary supplements and nutrients, other supplements, and drugs.
- Identify and facilitate the development of new methods for characterizing supplements and their active components.
- Establish guidelines to delineate the combination of experimental methods necessary to demonstrate high confidence levels for efficacy and safety of dietary supplement use.

**Goal 5: Inform and educate scientists, health care providers, and the public about the benefits and risks of dietary supplements.**

The ODS Director was mandated by Congress [Public Law 103-417, Section 13.(a)] to serve in an advisory capacity to the Department of Health and Human Resources regarding "(A) dietary intake regulations; (B) the safety of dietary supplements, (C) claims characterizing the relationship between (i) dietary supplements; and (ii) (I) prevention of disease or other health-related conditions; and (II) maintenance of health; and (D) scientific issues arising in connection with the labeling and composition of dietary supplements." *The Report of the Commission on Dietary Supplement Labels* recommends that the ODS place greater emphasis on this advisory role. The ODS has included this mandate as a specific objective for achieving goal 5.

Since the ODS began in November 1995, the office has received over 1,200 calls or requests from the public for personal health care information about dietary supplements. An almost equal number of calls have been logged in the ODS from scientists and health care professionals. To assist these groups, the ODS will promote and support the development of scientifically valid information and educational materials.

The following objectives address Goal 5:

- Serve as a key resource and adviser for policy makers about dietary supplements.[*]
- Develop and maintain a publicly accessible database of published, peer-reviewed, scientific literature on dietary supplements.*

[*] Specific areas of scientific priority included in the DSHEA legislation.

- Develop and maintain a publicly accessible database of federally funded scientific research on dietary supplements.*
- Stimulate dialogue about dietary supplements among government agencies, academia, public advocacy groups, and industry.
- Facilitate the integration of scientific information on dietary supplements within standard and continuing education programs for health care providers.
- Promote training of scientific investigators in dietary supplements research, as well as effective communication of research results.
- Encourage the regular inclusion of dietary supplement intake information as part of a patient's medical history.
- Conduct a survey to assess the need for a public information system on dietary supplements.
- Evaluate and effectively communicate to the public the results of recent scientific research.

Office of Dietary Supplements
Office of the Director
National Institutes of Health

NIH Publication No. 99-4365
September 1998

# Appendix C
# ODS Research Enhancement Awards Program (REAP)

| Project Title | Principal Investigator(s) | Institution | NIH Institute |
|---|---|---|---|
| **INITIATED in 1998** | | | |
| Tryptophan and Native American Alcoholism (second award) | Walter R. Adams, Ph.D. | Brown University<br>Providence, RI | NIAAA |
| Chronic Dental Disease and Cardiovascular Disease | Kaumudi Joshipura, BDS, D.Sc. | Harvard University<br>School of Dental Medicine<br>Cambridge, MA | NIDCR |
| Modulation of Olfactory Circuits | Paul Q. Trombley, Ph.D. | Florida State University<br>Tallahassee, FL | NIDCD |
| Zinc Kinetics in Metallothionein Knockout Mice | Meryl Wastney, Ph.D. | Georgetown University<br>Medical School<br>Washington, DC | NIDDK |
| **INITIATED in 1997** | | | |
| Oxidative Damage in Sugar-Induced Cataractogenesis | Naseem Ansari, Ph.D. | University of Texas Medical Branch<br>Galveston, TX | NEI |
| Metabolic Implication of Dietary Arginine Supplements | Peter J. Garlick, Ph.D. | State University of New York<br>Health Sciences Center<br>Stony Brook, NY | NCI |
| Parenteral Nutrition and Mucosal Amino Acid Metabolism | Peter J. Reeds, Ph.D. | Baylor College of Medicine<br>Houston, TX | NICHD |
| **INITIATED in 1996** | | | |
| Mechanisms of Antibiotic-Induced Hearing Loss | Jochen Schacht, Ph.D. | University of Michigan<br>Ann Arbor, MI | NIDCD |

| | | | |
|---|---|---|---|
| Vanadium Salts and Carbohydrate Metabolism in Humans | Harry Shamoon, M.D. | Albert Einstein College of Medicine<br>New York, NY | NIDDK |
| Brain MR Spectroscopic Studies of Thiamine Deficiency | Haakil Lee, Ph.D. | Vanderbilt University Medical Center<br>Nashville, TN | NINDS |
| Mechanisms of Anti-Folate Efficacy in Arthritis | Sarah L. Morgan, M.D., Ph.D. | University of Alabama<br>Birmingham, AL | NIAMS |
| Tryptophan and Native American Alcoholism | Walter R. Adams, Ph.D. | Brown University<br>Providence, RI | NIAAA |
| Bone Density Loss in Athletes | Robert Klesges, Ph.D. | University of Memphis<br>Memphis, TN | NIAMS |

# Appendix D

## ODS-Supported Workshops and Conferences

| Topic of Meeting | NIH Sponsor | Date |
|---|---|---|
| The Effect of Dietary Supplements on Craniofacial Development | NIDCR | Planned 1999 |
| Dietary Supplements for Wasting | NIAID<br>NIDDK | Planned 1999 |
| The Effect of Dietary Supplements on the Impact of Infectious Diseases on the Oral Cavity | NIDCR | Planned 1999 |
| Phytoestrogen Use in Middle-Aged and Older Women | NIA | Planned<br>Summer 1999 |
| Micronutrients: Their Role in the Pathophysiology, Immunopathology, Treatment, and Prevention of Tropical Infectious Diseases | NIAID | Planned<br>Apr 1999 |
| Nutritional Implications of Cephalic Phase Responses | NIDCD | Planned<br>Apr 1999 |
| Zinc and Health: Current Status and Future Directions<br>Zinc: What Role Might Supplements Play? | ODS<br>+ 6 Institutes and Centers | Nov 4-6, 1998 |
| Emerging Issues in Microbial Infections and Cardiovascular Disease | NIAID | Oct 29-30, 1998 |
| International Workshop to Evaluate Research Needs on the Use and Safety of Medicinal Herbs | NIEHS | Sept 22-23, 1998 |
| Factors Influencing the Need for Dietary Supplements for Pregnancy | NICHD | Sept 16-17, 1998 |
| Essential Fatty Acids in the Treatment of Mental Disorders | NIAAA, NIMH | Sept 2-3, 1998 |
| Role for Coenzyme $Q_{10}$ in the Aging Process: Potential Benefits of $Q_{10}$ Supplementation | NIA | Aug 31-<br>Sept 1, 1998 |
| Metabolic, Endocrine and Gastrointestinal Disorders in Drug Abuse and HIV/AIDS | NIDA | Aug 3-4, 1998 |
| Folic Acid, Vitamin $B_{12}$, and One Carbon Metabolism, FASEB | NIDDK | Aug 1-6, 1998 |
| Human Selenium Deficiency and Approaches to Intervention | FIC<br>NCI | Jun 16-19, 1998 |
| Nutritional and Health Benefits of Inulin and Oligofructose Conference | - | May 18-19, 1998 |
| The Path to Maternal and Child Health: The PVO Role in Improving Iron and Vitamin A Status | FIC | May 5-7, 1998 |
| Lutein and Zeaxanthin: Safety and Procedural Issues for Supplementation in Relation to the Development of Macular Degeneration | NEI | Feb 10, 1998 |

| | | |
|---|---|---|
| Frontiers in Antioxidant Research, ASPEN 1998 Research Workshop | NIDDK | Jan 18, 1998 |
| Role of Dietary Supplements in Brain Function | ODS-initiated poster workshop | Jul 29, 1997 |
| Role of Botanical Supplements in Health: Recent Research Advances and Directions | ODS-initiated poster workshop | Jul 29, 1997 |
| Phospholipids in Health and Disease | - | Sept 8-10, 1996 |
| Melatonin and Aging | NIA | Aug 14-16, 1996 |
| Melatonin and Sleep | NIA | Aug 12-13, 1996 |
| Dietary Supplements for Physically Active People | ODS + 11 Institutes and Centers | Jun 3-4, 1996 |
| Genetic and Environmental Determinants of Copper Needs Across the Life Span | FIC | Mar 18-19, 1996 |
| Approach to the Prevention of Orofacial Cleft | NIDCR | Mar 17-18, 1996 |

# Appendix E
# ODS Grant-Supported or Staff Publications


Adams, W.R., Holder, S.R., Teufel, N.A., Duncan, D., Harrison, F., Miller, B.L. and Wauahdooah, B. (1998) The impact of tryptophan, vitamin B6, ascorbic acid, and zinc intake on alcohol use in an Oklahoma Native American tribe." Alcohol and Drug Study Group Bulletin 34(1):10-13.

Adams, W.R., Teufel, N.A., Holder, S.R., Duncan, D., Harrison, F., Miller, B.L. and Wauahdooah, B.. The tryptophan-serotonin complex and alcohol use in an Oklahoma native american tribe. (submitted for publication)

Aharon, Y., Mevorach, M., Rossetti, L. and Shamoon, H. (1998) Vanadyl sulfate does not enhance insulin action in patients with type I diabetes. *Diabetes Care* 21:2194-2195.

Aharon, Y., Mevorach, M. and Shamoon, H. (1997) Vanadyl sulfate does not enhance insulin action in patients with IDDM. *Diabetes* 46(suppl 2):95A.

Ansari, N.H., Zhang, W., Fulep, E. and Mansour, A. (1998) Prevention of pericyte loss by trolox in diabetic rat retina. *J. Toxicol. Environ. Health* 54:467–475.

Baggott, J.E., Morgan, S.L. and Koopman, W.J. (1998) The effect of methotrexate and 7-OH methotrexate on rat adjuvant arthritis and on urinary aminoimidazole carboxamide excretion. *Arthritis Rheum.* 41:1407–1410.

Baggott, J.E., Morgan, S.L., Sams, W.M. and Linden, J. Urinary adenosine and aminoimidazolecarboxamide excretion in methotrexate-treated psoriasis patients. (submitted for publication)

Caso, G., McMillan, D.N., Eremin, O. and Garlick, P.J. Arginine and the growth of human breast tumor cells in culture. (in preparation)

Cohen, N., Halberstam, M., Shlimovich, P., Chang, C.J., Rossetti, L. and Shamoon, H. (1996) Oral vanadyl sulfate improves hepatic and peripheral insulin sensitivity in NIDDM but not in obese nondiabetic subjects. *Diabetes* 45:659-666.

Eck, L.H., Klesges, R.C., Ward, K.D., Shelton, M.L., Slawson, D.L., Cantler, E.D. and Vukadinovich, C.M. Sources of calcium intake in a sample of African-American and Euro-American collegiate athletes. *J. Nutr. Ed*. (in press)

Garlick, P.J., McNurlan, M.A. and Caso, G. (1998) Critical assessment of methods used to measure protein synthesis in human subjects. *Yale J. Biol. Med*. 70:65-76.

Garlick, P.J., McNurlan, M.A. and Caso, G. (1997) Protein turnover in cancer patients. Pp.85–101 in: *Gene Expression and Nutrition in Animals: From Cells to Whole Body*, Muramatsu, T., ed., Trivandrum, India: Research Signpost.

Glazer, A., Scannell, K.M., Costello, R.B., Krakower, T.J. and Marriott, B.M., compilers. (1998) *Zinc and health* [bibliography on the Internet]. Bethesda (MD): National Library of Medicine, 1998 Oct. (Current bibliographies in medicine; no. 98-3). 3619 citations from January 1990 through June 1998. Available from: http://www.nlm.nih.gov/pubs/resources.html.

He, Q., Khanna, P., Srivastava, S., van Kuijk, F.J.G.M. and Ansari, N.H. (1998) Reduction of 4-hydroxynonenal and 4-hydroxyhexenal by retinal aldose reductase. *Biochem. Biophys. Res. Comm*. 247:719–722.

Institute of Medicine (IOM) (1998) *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin $B_6$, Folate, Vitamin $B_{12}$, Pantothenic Acid, Biotin, and Choline*. National Academy of Sciences, Food and Nutrition Board. Washington, D.C.: National Academy Press.

Kaufman, E.M. and Klesges, R.C. (1998). Does gaining weight prevent osteoporosis? An evaluation of the relationship between body fat, muscle mass, and bone density. *Ann. Behav. Med*. 20:S204.

Khanna, P., Wang, L., Perez-Polo, R.J. and Ansari, N.H. (1997) Oxidative defense enzyme activity and mRNA levels in lenses of diabetic rats. *J. Toxicol. Environ. Health*. 51:541-555.

Klesges, R.C., Ward, K.D., Palmieri, G.M.A., Applegate, W.B., Cantler, E.D. and Harmon-Clayton, K. (1996). Risk of exercise induced bone mineral loss in different team sports. *J. Bone Min. Res.* 11(suppl 1):654.

Lamberg, L. (1996) Melatonin potentially useful but safety, efficacy remain uncertain. *J. Am. Med. Assoc*. 276(13):1011-1014.

Lautermann, J. and Schacht, J. (1996) A sensitive animal model to assess acute and chronic ototoxic effects. *Arch. Otolaryngol. Head Neck Surg*. 122:837–840.

Lönnerdal, B. and Uauy, R., eds. (1998) Genetic and environmental determinants of copper metabolism. Proceedings of an international conference held in Bethesda, MD, March 18-20, 1996. *Am. J. Clin. Nutr*. 67:5(S).

Marriott, B.M. (1997) Vitamin D supplementation: a word of caution. *Ann. Int. Med*. 128(3):231-233.

Marriott, B.M. and Kanter, M., eds. (1998) The role of dietary supplements for physically active people. *Am. J. Clin. Nutr*. (in press).

Morgan, S.L., Baggott, J.E. and Alarcon, G.S. (1997) Methotrexate in rheumatoid arthritis. Folate supplementation should always be given. *BioDrugs* 8(3):164-175.

Morgan, S.L., Baggott, J.E., Lee, J.Y. and Alarcon G.S. (1998) Folic acid supplementation prevents deficient blood folate levels and hyperhomocysteinemia during long-term, low dose methotrexate therapy for rheumatoid arthritis: Implications for cardiovascular disease prevention. *J. Rheumatol*. 25: 441-446.

Morgan, S.L., Baggott, J.E., Lee, J.Y. and Alarcon, G.S. (1997) Folic acid prevents elevated homocysteine (hcy) levels during methotrexate (MTX) therapy. *Arthritis Rheum.* 40:S53.

Morgan, S.L. and Weinsier, R.L., eds. (1998) *Fundamentals of clinical nutrition,* 2d ed. St. Louis, MO.: Mosby

Peterson, B.A., Klesges, R.C., Kaufman, E.M., Cooper, T.V. and Vukadinovich, C.M. (1998) Calcium intake and bone content in young women. *Ann. Behav. Med.* 20:S213.

Reeds, P.J., Burrin, D.G., Stoll, B. and Jahoor, F. Intestinal glutamate metabolism. *J. Nutr*. (submitted for publication)

Scannell, K.M., Marriott, B.M. and Costello, R.B. (1995). *The role of dietary supplements for physically active people: January 1966 through April 1996.* U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Library of Medicine, Reference Section, Pittsburgh, PA.

Schacht, J. Antioxidant therapy attenuates aminoglycoside-induced ototoxicity. *Ann. NY. Acad. Sci*. (in press)

Sha, S-H. and Schacht, J. Mechanism and prevention of aminoglycoside-induced hearing loss. In: *Cell and Molecular Biology of the Ear,* Lim, D.J., ed., New York: Plenum Press. (in press)

Sha, S-H. and Schacht, J. (1998) Are aminogylcoside antibiotics excitotoxic? *NeuroReport* 9:3893-3895.

Sha, S-H. and Schacht, J. (1998) Formation of reactive oxygen species following bioactivation of gentamicin. *Free Radical Biol. Med.* 26:341-347.

Sha, S-H. and Schacht, J. (1998) Are aminoglycoside antibiotics excitotoxic? *NeuroReport* 9:3893-3895.

Song, B–B. and Schacht, J. (1996) Variable efficacy of radical scavengers and iron chelators to attenuate gentamicin ototoxicity in guinea pig *in vivo*. *Hear. Res.* 94:87–93.

Song, B-B., Sha, S-H. and Schacht, J. (1998) Iron chelators protect from aminoglycoside-induced cochleo- and vestibulotoxicity in guinea pig. *Free Radical Biol. Med.* 25:189–195.

Stoll, B., Burrin, D.G., Henry, J., Yu, H., Jahoor, F. and Reeds, P.J. Substrate oxidation by the portal drained viscera of fed piglets. *Am. J. Physiol.* (submitted for publication)

Tamura, T., Bergman, S.M. and Morgan, S.L. (1998) Hyperhomocysteinemia as a cause of vascular thrombosis in patients with end-stage-renal disease. *Int. J. Artif. Organs* 21:72–74.

Ward, K.D., Klesges, R.C., McClanahan, B., Harmon-Clayton, K., Fallone, G., Cantler, E., Palmieri, G.M.A. and Applegate, W.B. (1997). Are extremely physically active people at risk for decreases in bone mineral density? A large-scale prospective investigation. *Ann. Behav. Med.* 19:S112.

Zhang, W., Khanna, P., Chaan, L.N., Campbell, G. and Ansari, N.H. (1997) Diabetes-induced apoptosis in rat kidney. *Biochem. Mol. Med*. 61:58–62.