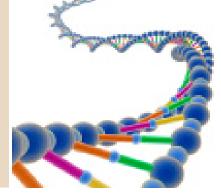


# Office of Dietary Supplements – Research Overview and Strategic Planning



Paul M. Coates Director, ODS

**DPCPSI Council of Councils June 2015** 





#### **Outline**

- A history of (dietary supplement) time
- Patterns of dietary supplement use in the US
- ODS programs to address needs in dietary supplement research
- ODS resources for consumers
- Strategic planning

#### **DSHEA:**

The Dietary Supplement Health and Education Act of 1994



- Amended the Food, Drug, & Cosmetic Act
- Defined dietary supplements (DS)
- Established regulatory framework
  - Food and Drug Administration (FDA)
  - As foods, not as drugs
- Established rules for what a label should contain
- Gave FDA authority to write DS-specific Good
   Manufacturing Practices
- Created the Office of Dietary Supplements at NIH

## Dietary Supplement: DSHEA Definition

- Product intended to supplement the diet
- Contains one or more of the following:
  - Vitamin
  - Mineral
  - Amino acid
  - Other dietary substance
  - Herb or other botanical (not tobacco)
- Not a conventional food
- Not intended to cure, treat, mitigate...

# Dietary Supplement Regulation

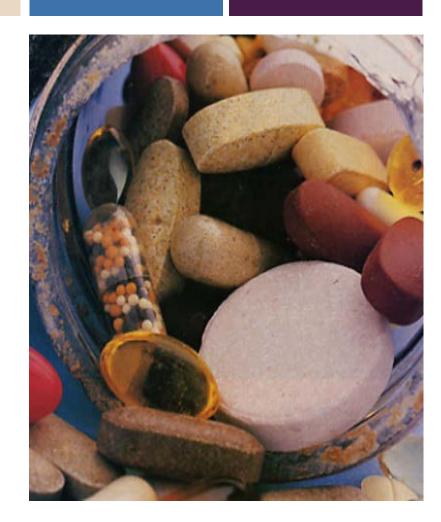




- Regulated more like foods than drugs
  - No need to register products with FDA or get prior approval
  - Don't have to be proven effective or safe
  - No mandatory formulation standards
  - Some assurance required for new (post 1994) ingredients
- FDA must prove "a significant or unreasonable risk of illness or injury" to ban supplement
- FDA post-marketing activities: monitoring product information and safety
- FTC regulates advertising
- Cannot make disease prevention or treatment claims, but can make other claims (e.g., "health promotion", "structure-function")

## What are They?

- Micronutrients
  - vitamins & minerals
- Macronutrients
  - fatty acids (ALA, EPA, DHA), protein & amino acids
- Herbs (botanicals)
  - St. John's wort, ginkgo
- Phytochemicals
  - lycopene, isoflavones
- Zoochemicals
  - creatine, CLA, bee pollen
- Miscellaneous items
  - probiotics, glucosamine, melatonin



## U.S. Supplement Sales (\$ Billions)

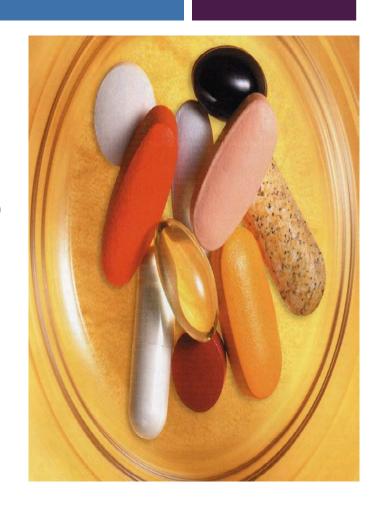
Products: 1994: 4,000 2015: 85,000?



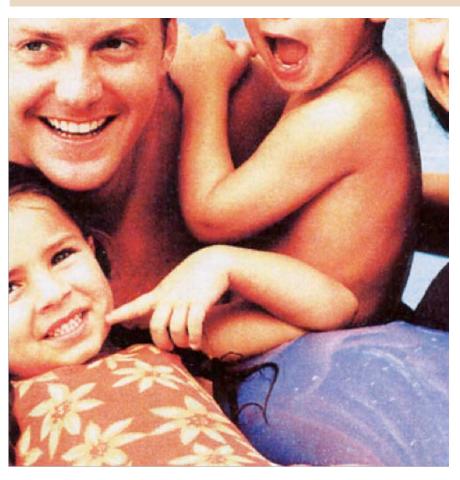
Source: Nutrition Business Journal

# **Extensive Supplement Use**

- ➤ 1/3 to 1/2 of U.S. population takes them daily or most days
- Most take 1-2 supplements/day (multis); others take dozens (light vs. heavy users)
- Most supplement moderately (RDA levels); some take megadoses
- Many supplement primarily with nutrients; others more adventurous



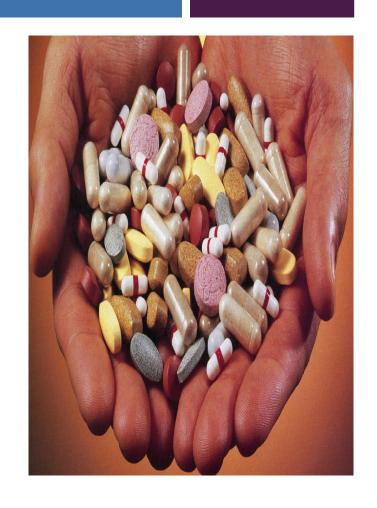
## **Most Likely Users**



- Women > men
- Older > younger
- Wealthier > poorer
- Healthy lifestyles > those with less healthy ones

#### **Reasons for Use**

- Nutritional insurance
- Optimal health
  - Possibly feel better
  - Systems working better (immunity, digestion, nervous system)
  - More disease resistant (heart disease, cancer, aging)
- Special purposes
  - Treatment of health problems & diseases
  - Performance enhancement





# ODS Mission - Strengthen Knowledge and Understanding of Dietary Supplements

- Evaluate Scientific Information
- Stimulate and Support Research
- Disseminate Research Results
- Educate the Public to Foster an Enhanced Quality of Life and Health for U.S. Population



# ODS Evidence-Based Review Program

- Systematic review of efficacy and safety of dietary supplements
- Collaboration with the Agency for Healthcare Research and Quality (AHRQ) Evidence-Based Practice Center Network
- Major reason: assist NIH in the development of research agendas
- Examples (partners): ephedra (NCCAM, FDA), omega-3 fatty acids (multiple), soy (NCCAM), probiotics (NCCAM, FDA); vitamin D and calcium (multiple)

http://ods.od.nih.gov/Research/Evidence-Based\_Review\_Program.aspx

### Health Effects of Omega-3 Fatty Acids 2004 – 2005

- Asthma
- Cancer
- Cardiovascular Disease and Risk Factors
- Arrhythmogenic Mechanisms
- Child and Maternal Health
- Cognitive Function
- Eye Health
- Type II Diabetes, Rheumatoid Arthritis, and Other Diseases
- Mental Health
- Organ Transplantation

# Omega-3 Fatty Acids, cont.

- Exposures
  - EPA, DHA, ALA
  - Dietary supplements and foods (fish and vegetable oils)
- Studies
  - CVD > child/maternal health > mental health
  - Fish oil > Fish diets > ALA
  - 4 good quality; 4 poor quality

# Omega-3 Fatty Acids, cont.

- Evidence generally inconclusive
  - Paucity of high quality studies
  - Heterogeneity of interventions
  - Conflicting findings
- Secondary prevention of CVD
  - Evidence → health benefit of fish oil/fish
- Adverse events
  - Appear to be minor
  - Only 1/3 had information
  - Incomplete and inadequate reporting

#### Dietary Supplement Research Product Concerns





Identification
Characterization
Contamination
Reproducibility





#### The ODS Role in Methods

#### U.S. Senate language beginning 2001

- Called for ODS to enhance collaborative efforts to develop and disseminate validated analytical methods and reference materials for the most commonly used botanicals and other dietary supplements
- ODS created Analytical Methods and Reference Materials Program (AMRM) in 2002

#### **AMRM Overview**

- Program designed for public/private partnership
  - Establish priorities (botanicals and others)
  - Identify potential research partners
- Develop, validate, share analytical methods
- Produce, share reference materials
- Applications
  - > Research: characterization of test substances
  - Industry: implementation of GMPs/product formulation
  - Regulators: label claims, safety

#### **NIST Standard Reference Materials®**

- Matrix Reference Materials systematically characterized raw materials and finished products
- Calibration Standard Solution SRMs
- Plant identity SRM (DNA verified) in progress
- SRMs for vitamin D metabolites in serum
- Other nutrient status biomarkers in progress

http://www.nist.gov/srm/index.cfm

## Laboratory Quality Assurance Programs

- Quality Assurance Program for analysis of dietary supplements in products
- Quality Assurance Program for measurement of vitamin
   D metabolites in serum
- Quality Assurance Program for omega-3s in serum

http://www.nist.gov/mml/analytical/qaps.cfm

# Vitamin D Becomes Public Health Focus

- Many receptors for vitamin D in body why?
- Limited controlled studies most evidence comes from observational studies
- Limited information on dose response
- Limited information on safety
- Advocates: Cancer, diabetes, CVD, immune function
- Declarations of widespread deficiencies
- Focus on increased supplement use

## ODS Supports and Leads Exploration of Issues Surrounding Vitamin D



2008+: Analytical Methods and Reference Materials for Vitamin D Assays

2009: AHRQ Systematic Review - Vitamin D and Health Outcomes

2010: IOM Review of DRIs for Vitamin D and Calcium

2010+: Vitamin D Standardization Program (VDSP)

2014: Updated Systematic Review -> Workshop on Issues for Primary Care Physicians



# Vitamin D Standardization Program (VDSP)





## **VDSP Objectives**

- To standardize 25-hydroxyvitamin D [25(OH)D] values in national health surveys to the U.S. NIST SRM 2972 and its Reference Measurement Procedure (RMP)
- To develop a research program on 25(OH)D and the laboratory standardization of its measurement
- To expand standardization services to include assay manufacturers and clinical and research laboratories
- To enable the use of standardized data in patient care and public health activities



## **ODS/VDSP Achievements**

- Developed VDSP Reference Measurement System
  - Laboratory reference methods for key metabolites of vitamin D
  - Standard Reference Materials
- Collaborated with CDC to develop their Vitamin D Standardization-Certification Program
- Collaborated with assay manufacturers to encourage assay standardization
  - Inter-laboratory comparison study
  - Commutability study
  - The five leading commercial assays have been standardized



## **ODS/VDSP** Achievements

- Collaborated with NIST and DEQAS to develop the world's largest laboratory testing system for 25(OH)D
- Developed models to standardize vitamin D values in previously conducted studies
- Standardized measurement of 25(OH)D in six national health surveys around the world: Australia, Canada, Germany, Ireland, UK, and USA

### NIH Botanical Research Centers Program



- 1999-2005
  - 2-6 Centers: ODS, NCCAM\*, others
  - Broad research goals + training + education
- 2006-2010
  - 6 Centers: ODS, NCCAM, others
  - Focus on pre-clinical and early clinical research
- 2010-2015
  - 5 Centers: ODS, NCCAM, others
  - Emphasis on developing new methodologies
  - Breast and prostate Ca, metabolic syndrome, women's health, inflammation
- 2015-2020
  - http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-14-001.html

<sup>\*</sup>NCCAM is now known as NCCIH: National Center for Complementary and Integrative Health



# ODS and the Broader NIH Supplement Research Portfolio

- Funding and co-funding for investigatorinitiated research across NIH ~ 50% of ODS budget
- Partnerships with other agencies-
  - ODS partnership with National Institute of Standards and Technology (NIST) supports development of analytical methods, standard reference materials and laboratory quality assurance programs
  - USDA, FDA, CDC (NHANES, etc.)
- Contracts and other mechanisms (DSLD)

# Nutrition and Dietary Supplement Interventions for Inborn Errors of Metabolism (NDSI-IEM)



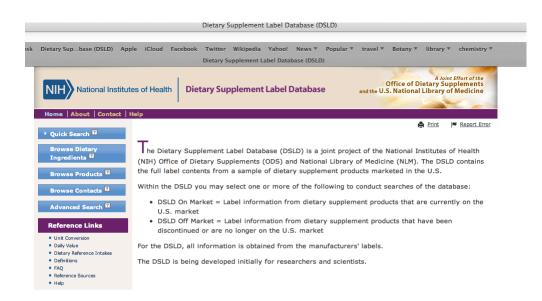
- Collaborations
  - NIH ICs, HRSA, FDA, researchers, clinicians, patient advocates, and industry representatives
  - International
- Identify gaps in safety and effectiveness of these therapies
  - Convened conferences and workshops
- Publish multi-authored review articles and conference proceedings
- Support clinical guideline development by professional organizations through these activities

# NDSI-IEM Conferences and Workshops

- Nutritional Interventions in Primary Mitochondrial Disorders,
   December 2014
  - Sponsors: ODS, ORDR/NCATS, UMDF, Wellcome Trust
  - A number of collaborative efforts are underway
- NIH Phenylketonuria Scientific Review Conference, February 2012
  - Sponsors: NICHD, ODS, ORDR/NCATS
  - Conference proceedings published in 2014
  - Informed medical and nutritional guideline development by ACMG and GMDI

## Dietary Supplement Label Database: ODS and NLM <a href="http://www.dsld.nlm.nih.gov/dsld/">http://www.dsld.nlm.nih.gov/dsld/</a>

- Launched in 2013
- Expect to include labels of virtually all dietary supplements sold in the US
- Photos of labels
- Searchable fields
- Publicly available
- 43,000 labels (May 2015)
- Adding 1,000 labels/month



Disclaimer: All information contained in the Dietary Supplement Label Database comes from dietary supplement labels. The dietary supplement label may not have met the then current nor meet current U.S. Food and Drug Administration (FDA) regulations. The presentation of dietary supplement label information is not an endorsement or guarantee of accuracy by the Office of Dietary Supplements or the National Library of Medicine, both part of the National Institutes of Health, U.S. Department of Health & Human Services.

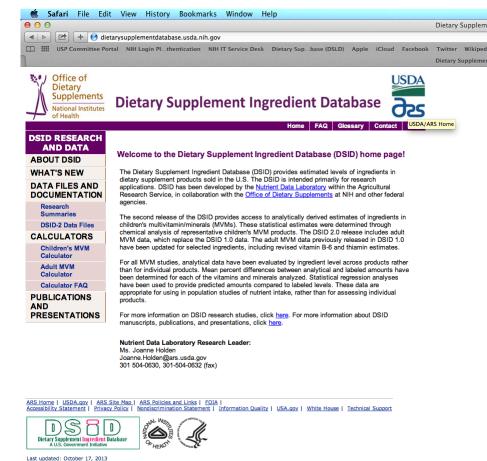
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#### **Dietary Supplement Ingredient Database: ODS and USDA**

http://dietarysupplementdatabase.usda.nih.gov

- Analytically verified dietary supplement labels for purposes of estimating nutrient exposure
- Two exercises to date:
  - Adult MVM
  - Children's MVM
- Next exercise to include a botanical product
  - Green Tea Extracts



#### **ODS Resources for Consumers**

Office of Dietary Supplements (ODS)



U.S. Department of Health & Human Services

National Institutes of Health



Strengthening Knowledge and Understanding of Dietary Supplements Font Size



Health Information

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#### INFORMACIÓN EN ESPAÑOL

Varias hojas informativas sobre ingredientes específicos de los suplementos dietéticos ahora están disponibles en español.

Several consumer fact sheets about individual dietary supplement ingredients are now available in Spanish.

#### **Health Information**

- > Frequently Asked Questions (FAQ)
- > Dietary Supplements: What You Need to Know
- > FDA: Warnings and Safety Info
- Información en español more

#### **Dietary Supplement Fact Sheets**

The Office of Dietary Supplements (ODS) fact sheets give a current overview of individual vitamins, minerals and other dietary supplements. ODS has fact sheets in two versions-Health Professional and QuickFacts. Both versions provide the same types of information but vary in the level of detail. QuickFacts are now available in Spanish. more

#### **General Information**

- **Background Information**
- **Botanical Dietary Supplements**
- Full List of Fact Sheets
- > Frequently Asked Questions
- > Información en español more

#### Featured Dietary Supplement Fact Sheets



#### Selenium

Selenium is found naturally in many foods, including seafood, more



Magnesium

The amount of magnesium you need depends on your age and sex, more

#### **News & Events**

#### HEADLINES

> Funding Available for Validation Studies of Analytical Methods more

#### KEEP UP TO DATE

- Sign up for the ODS listsery
- > Read the ODS newsletters
- Access free ODS mobile app, MyDS
- Follow us on Facebook &
- Follow us on Twitter
- Share/Bookmark



#### **VITAMIN E QUICKFACTS**



Many foods have vitamin E including vegetable oils (such as wheat germ, sunflower, and safflower oils), nuts (such as almonds), seeds (such as sunflower seeds), and green vegetables (such as spinach and broccoli).

Vitamin E is a fat-soluble nutrient found in many foods. In the body, it acts as an antioxidant, helping to protect cells from the damage caused by free radicals. Free radicals are compounds formed when our bodies convert the food we eat into energy. People are also exposed to free radicals in the environment from cigarette smoke, air pollution, and ultraviolet light from the sun.

The body also needs vitamin E to boost its immune system so that it can fight off invading bacteria and viruses. It helps to widen blood vessels and keep blood from clotting within them. In addition, cells use vitamin E to interact with each other and to carry out many important functions.

#### How much vitamin E do I need?

The amount of vitamin E you need each day depends on your age. Average daily recommended intakes are listed below in milligrams (mg) and in International Units (IU). Package labels list the amount of vitamin E in foods and dietary supplements in IU.

Birth to 6 months	4 mg	(6 IU)
Infants 7–12 months	5 mg	(7.5 IU)
Children 1-3 years	6 mg	(9 IU)
Children 4-8 years	7 mg	(10.4 IU)
Children 9–13 years	11 mg	(16.4 IU

### Summary





- Challenges in doing research with dietary supplements
  - Many ingredients, many issues
  - Strongly held beliefs
  - For nutrients: background diet, health outcomes
  - For interventions: experimental design, product characterization
- Resources
  - NIH, USDA, NIST, CDC, others

### **ODS Strategic Planning**

- ODS guided by successive strategic plans since 1999
- Emphasis has always been on 3 things: research, resources for investigators, resources for consumers
- These are reflected in the nearly-completed plan for 2015-2020
- Process
  - Progress report for agency and public input: January 2015
  - Draft plan for input: July 2015
  - Release final plan: Fall 2015
  - Continuously monitor progress



Website: <a href="http://ods.od.nih.gov">http://ods.od.nih.gov</a>

Email: <a href="mailto:ods@nih.gov">ods@nih.gov</a>