

FY2013 REFERRAL GUIDELINES THE OFFICE OF DIETARY SUPPLEMENTS (ODS)

These referral guidelines have been prepared for use by NIH and other Agencies in determining projects within the scope of the Office of Dietary Supplements. The mission of the Office of Dietary Supplements (ODS) is to support both basic and applied research as well as research training and other programs to foster an understanding of dietary supplements in health maintenance and disease prevention.

Research interests of ODS are not limited to specific health conditions, organ systems or populations groups. ODS supports all types of research, including pre-clinical, clinical, behavioral, and epidemiological, *in which the primary emphasis is the investigation of dietary supplements and/or their ingredients**. Additionally, ODS supports research and training programs that build future research capacity for studying the role of dietary supplements in health and disease prevention.

Primary consideration for support will be given to proposals that stimulate dietary supplement research where it is lacking or lagging, clarify gaps, opportunities and balance between benefits and risks where data are in conflict, target special population groups where additional science on supplements is needed, and focus on the use of supplements in improving or maintaining health and reducing the risk of chronic disease.

Due to constrained budgets, ODS mission-relevant research will be focused on the above bulleted areas. For FY2013, ODS will not entertain grants that have disease treatment as a focus.

Examples of research projects that fall within the mission of ODS include but are not limited to:

- Evidence-based evaluations of the role of dietary supplements, including evaluation of the safety and efficacy of supplement use in the prevention and reduction of risks for chronic diseases.
- Intervention studies that examine the effects of dietary supplements on maintenance of optimal health or reduction of disease risk where supplement interventions alter, physiological endpoints or other health outcomes (e.g., a study that examines the physiologic or mechanistic effects of St. John's wort on depression or a study assessing the effects of calcium supplements on bone mass density and the reduced risk of osteoporosis).

*As defined by Congress in the 1994 Dietary Supplement Health and Education Act a dietary supplement is a product (other than tobacco) that is intended to supplement the diet; contains one or more dietary ingredients (including vitamins; minerals; herbs or other botanicals; amino acids; and other substances) or their constituents; is intended to be taken by mouth as a pill, capsule, tablet, or liquid.

- Observational studies that examine the association between intakes of nutrients or other substances from supplementation and disease risk, physiological endpoints or other health outcomes. These would include studies that use food frequency questionnaires, diet recalls, diet records, diet histories, diet surveys and other dietary assessment methods (e.g., a study that uses a food frequency questionnaire to analyze associations between intakes of vitamin E and phytoestrogens and breast cancer risk). Studies that focus on the beneficial or adverse interactions of dietary supplements with foods, drugs, and other dietary supplements in healthy persons and those with selected conditions where these interactions may affect disease prevention, risk reduction, or the promotion of health and well-being.
- Studies that investigate isolated bioactive compounds from foods to determine their safety or effect on disease risk, physiological endpoints or other health outcomes, even if they are not currently available as dietary supplements (e.g., a study to investigate bioactive compounds in human milk that are involved in infant growth and development or a study to investigate the safety of phytochemicals from mushrooms or their effects on host immunity or metabolism).
- Studies that examine the safety, form or bioavailability of dietary supplements (e.g., a rodent study to examine the safety of high intakes of vitamin A, a human study to examine the bioavailability of various forms of folic acid, or a clinical trial to examine the safety and side effects of various doses of saw palmetto).
- Studies that delineate how dietary supplements moderate, alter or enhance metabolic, physiological or psychological processes associated with maintenance of optimal health and performance during the life cycle.
- Studies of single ingredients or complex mixtures that examine the transport, metabolism, mechanism of action, associated enzymes, binding sites, regulatory mechanisms or excretion of dietary supplements in order to elucidate their physiological or biochemical role (e.g., a study to investigate the transport and metabolism of orally administered folic acid or a study to evaluate the mechanism of action of the various components in *Panax ginseng*).
- Research to develop, evaluate, optimize or validate analytical methods for verifying ingredient identity and quantifying declared ingredients in raw materials and finished dietary supplement products.

Examples of research projects that typically fall outside the scope of ODS include:

- Studies that administer the supplement intervention with the sole intent to treat a disease process or outcome such as atherosclerosis or depression, without evaluation of the supplement's effect on the underlying mechanism of action, bioavailability or elucidation of metabolic pathways.

- Human, animal or laboratory studies that only correlate physiological levels of dietary supplements, their metabolites or marker compounds with disease risk, physiological endpoints or other health outcomes without the administration of a dietary supplement (e.g., a human study correlating serum levels of 25(OH) vitamin D and risk of hip fracture or a human study correlating serum levels of folate and cardiovascular disease).
- Studies evaluating the effect of whole foods that could be considered “functional foods.” This would include foods such as broccoli and other cruciferous vegetables, garlic, soy and flaxseed. However, if a food ingredient in a defined form is being investigated (e.g., a garlic capsule, a soy or phytoestrogen supplement, EGCG in a green tea supplement, or dried ginger root in a tea bag), then the study would be within the scope of ODS.
- Studies that involve dietary ingredients used to treat inborn errors of metabolism, such as a study investigating the use of tyrosine to treat phenylketonuria. However, if the research is focused on the mechanism of action, it could be considered within scope.
- Studies of compounds that are classified as drugs, such as the hormones estrogen, progesterone, and insulin.

As noted in the accompanying ICD Memo, FY2013 reviews will take place according to the following schedule:

ODS Receipt Date	ODS Review Date	Notification of Funding to IC
Nov. 19	Dec. 12	Dec. 28
Feb. 5	Feb. 20	March 1
April 30	May 15	May 30
July 30	Aug. 14	Aug. 23

Guidelines for Submission of Conferences and Workshops

A short description of the meeting(s) is necessary for the selection process. Please submit the description of your request on the attached form, "Format for Workshop/Conference Proposal Request, FY2013." The following information should be included:

- A tentative title.
- A brief summary of the purpose of the meeting.
- A general description, including the scope (national or international), size and format (workshop, small conference, symposium, forum, etc.).
- Description of target audience.
- Anticipated dates for the meeting.
- Possible outcomes (e.g., publications or proceedings).
- Budget information (specify the amount of funding requested from ODS).
- Draft agenda with potential speakers and topics.

If similar symposia on the proposed topic have been held within the past two to three years, please describe how the currently proposed symposium will differ. If you are nominating an R13 Conference Grant for sponsorship, please include the grant application and summary statement, if available.

If a conference or workshop is being developed by an Institute or Center at NIH, the ODS would like the opportunity to work closely with the IC program staff in the planning and development of this joint activity, with the goal of fostering a program and format that is productive and beneficial to program participants. Support for conferences, workshops, and symposia is typically in the range of \$2,500 to \$10,000, depending on the mechanism, focus, and level of ODS participation. ODS support is not intended to cover all expenses for a grant, conference or symposium.

All requests from your IC should receive IC Director approval prior to sending them to the ODS.

You or your program staff are encouraged to contact us in ODS to discuss potential conference funding opportunities. Direct inquiries and submit requests on the attached form to Cindy Davis in ODS at davisci@od.nih.gov by the review dates listed on the cover memo.

General Guidelines for Submission of Extramural and Intramural Projects

1. For studies investigating dietary supplements and/or supplement ingredients, the supplement should be administered in physiologically relevant forms and concentrations, and must be ingested in the oral form for clinical studies.
2. In studies employing dietary assessments or surveys, questions about dietary supplement use must be included and the survey instruments should be validated.
3. A rationale for how the proposed research fits within the mission of the ODS (See ODS Strategic Plan Goals at http://ods.od.nih.gov/About/about_ods.aspx).
4. Investigators conducting clinical studies must contact the FDA to determine if an Investigational New Drug (IND) is needed.
5. Information demonstrating that the dietary supplement adheres to the NCCAM Policy for Natural Products Integrity (an ODS summary of the policy is provided for your reference- See attached Minimum Criteria: Assessment of Dietary Supplement Ingredient Integrity) will be required prior to funding. Additional requirements for clinical trials, animal studies and probiotics can be found at the following website: <http://nccam.nih.gov/research/policies/naturalproduct.htm>).
6. For studies that measure 25(OH)D, the PI will be required to use National Institute of Standards and Technology (NIST) standard reference materials (add website) and are encouraged to participate in the NIST Vitamin D Metabolites Quality Assurance Program (<http://www.nist.gov/mml/analytical/vitdqap.cfm>). For large clinical trials, it is also recommended that the laboratory making the measurement participate in CDC's Vitamin D Certification Program (<http://www.cdc.gov/labstandards/hs.html>).
7. Analytic methods must be adequately described and must be demonstrated to be scientifically valid and suitable for their intended purpose.

All requests from your IC should receive IC Director approval prior to sending them to the ODS.

Specific Guidelines for Extramural Requests

Support for grants, including supplemental projects, will vary depending on the mechanism, relevance to ODS mission, and proposed costs. Support generally ranges from \$25,000 to \$200,000. The ODS typically supports out-year funding for grants pending satisfactory progress and availability of funds

Please email the following material to Cindy Davis at davisci@od.nih.gov:

- A copy of the e-summary statement and e-application responsive to General Guidelines 1 and 2 above, as applicable.
- A copy of the grant's e-abstract.
- A short memo highlighting the key points of the grant and relevance to the mission of ODS (1-2 pages), as well as incorporating the information in General Guidelines 3-7 above, as applicable.
- IC contact information

Applications received without all of the above will be returned.

If you require an ODS decision by a particular date, please specify that and we will do all we can to accommodate your needs. If multiple grants are submitted for consideration, please prioritize your list.

Specific Guidelines for Intramural Requests

ODS funding of intramural projects is designed for research projects that can be carried out in a short period of time with limited resources. *Priority will be given to young scientists accepted into the NIH Intramural Tenure-Track Program, Senior Staff Fellows or Postdoctoral Fellows with at least one year of postdoctoral research experience.* The proposal should be written by the trainee. Projects submitted for ODS co-funding should be within the Guidelines for the Conduct of Research in the Intramural Research Program at NIH (<http://sourcebook.od.nih.gov/ethic-conduct/Conduct%20Research%206-11-07.pdf>). **Intramural projects should be peer reviewed in accordance with individual Institute guidelines.**

In addition to the ODS General Guidelines (noted on page 5) additional intramural co-funding features include:

- Support is available for a variety of types of NEW projects including pilot or feasibility studies, collection of preliminary data, secondary data analysis of existing data, small, self-contained research projects, or development of new research technology. ODS co-funding is intended to stimulate new avenues of research within the NIH.
- Generally limited to one year of funding, not to exceed \$100,000. ODS funding is not meant to replace salary support currently being provided through an NIH post-doc stipend, but support for a postbac candidate will be considered.
- Generally not renewable.
- Completion of an annual progress and/or final report.

Intramural requests for support should include a description of the Research Plan, not to exceed 10 pages, including tables, graphs, figures, and diagrams and charts.

The Research Plan should include:

- Introduction (one page limit): Describe how this proposed study supports the ODS mission.
- Hypothesis under investigation.
- Background and significance.
- Clearly defined specific aims. Preliminary studies (if available).
- Research design and methods to include specific details on the chemical/biological composition and standardization of the intervention (dietary supplement as well as experimental diets)

Supporting documents, in addition to the 10-page Research Plan, should include:

- Budget
- Biosketches for the Principal Investigator (fellow) and mentor
- Two-page Training Plan (see below)
- Description of how this proposal was peer reviewed within the Institute/Center

Training Plan for Research Fellows

The candidate and the mentor are jointly responsible for the preparation of the training plan. The systematic plan must be designed to develop the necessary knowledge and research skills in scientific areas relevant to the young scientist's career goals. The sponsor/mentor may form an advisory committee to assist with the development of a program of study or to monitor the candidate's progress through the training.

The Training Plan, not to exceed two pages (excluding publications), should include:

- Candidate's objectives and long term career goals.
- A description of candidate's prior training and how it relates to candidate's objectives and long term career plans.
- A description of candidate's professional responsibilities in his/her current NIH research position.
- A description of candidate's research efforts to date, including any publications, prior research interests and experience.
- A statement of how the proposed new training and research experience logically evolves from prior training and experience and how it will facilitate the young scientist's transition to independent investigator status.
- Mentor's description of his/her oversight role in the training experience as well as expectations and deliverables for the trainee. Also note if other mentors will be engaged in the trainee's research.
- A timeline is helpful.
- An explanation of how research and educational resources of the institution will be utilized to promote candidate's independence.

Direct inquiries and submit requests to Cindy Davis, at davisci@od.nih.gov or 301-496-0168.

Minimum Criteria
Assessment of Dietary Supplement Ingredient Integrity
(Adapted from NCCAM Guidance on Biologically Active Agents)

- For botanicals, provide the correct, complete taxonomic/scientific name along with the common name.
- For non-botanical ingredients, a full description is required. This should include brand name (if given), chemical purity (and method determined), and isomeric purity.
- Identify the manufacturer or distributor (if any) by name and address and contact information along with product brand name, if applicable.
- State the constituent(s) to which the product is standardized.
- Characterize the supplement composition (ingredient content and quantity), if applicable.
- Provide documentation that demonstrates stability of ingredients for at least the duration of the study and explain how the product will be monitored for stability throughout the project period.
- Provide documentation that demonstrates reproducibility of product characteristics, especially if more than one batch is used in the study.
- Assure that the product is free of impurities (accidental or deliberate), e.g., pesticides, drugs, microbes, or metals.
- If the product is administered via a vehicle other than a tablet/capsule, assure that the characteristics remain stable and bioavailable (e.g., probiotic added to porridge, EGCG added to rat food).
- For placebo, verify that the product matches the test agent on sensory characteristics, that the sensory characteristics are stable, and that the product contains no bioactives.
- In general, assure that the investigator will be able to appropriately describe the intervention in results papers as described in Gagnier et al. (see below)

Reference Resources

- Gagnier JJ, Boon H., Rochon P et al. Reporting Randomized, Controlled Trials of Herbal Interventions: An Elaborated CONSORT Statement. *Annals of Internal Medicine*, 2006;144:364-367.
- Hildreth J, Hrabeta-Robinson E, Applequist W, Betz J, Miller J. Standard operating procedure for the collection and preparation of voucher plant specimens for use in the nutraceutical industry. *Anal Bioanal Chem*. 2007;389:13-17.
- NCCAM website and associated documents

Assessing product integrity

<http://nccam.nih.gov/research/policies/naturalproduct.htm>

Format for Workshop/Conference Proposal Requests FY2013

FOR RECEIPT ON: **Nov. 19** **Feb. 5** **April 30** **July 30**

Name of Scientific Workshop or Conference

Type of Event

- Workshop**
- Symposium**
- Conference**

National/International

Format and/or proposed Agenda

Background/History/Level of Peer Review

Brief Narrative Description of Event (approximately 1/2 - 1 page, single spaced)

- Purpose**
- Scientific Importance**
- Proposed Content**

Approximate Total Cost/Budget

Requested Amount from ODS

Proposed Dates(s) of Event

Proposed Location(s)

Organizer/Program Contact for More Information

- Name**
- Title**
- IC Program**
- Mailing Address**
- E-mail Address**
- Telephone Number**
- Fax Number**

Planned or Potential Outcomes

Other Potential Co-Sponsors

Potential Participants (Please provide copy of draft agenda and proposed speakers)