ORI DIETARY SUPPLEMENT STUDY FAQ

1. What are dietary supplements?

https://www.fda.gov/Food/DietarySupplements/

- A dietary supplement is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet.
- The "dietary ingredients" in these products may include: **vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, glandulars, and metabolites.**
- Dietary supplements can also be extracts or concentrates, and may be found in many forms such as tablets, capsules, softgels, gelcaps, liquids, or powders. They can also be in other forms, such as a bar, but if they are, information on their label must not represent the product as a conventional food or a sole item of a meal or diet.

Under the Dietary Supplement Health and Education Act (DSHEA) of 1994, a dietary supplement is not considered a drug and is not subject to the premarket approval requirements for drugs if the intended use is only to affect the **structure or any function** of the body (i.e., not for a therapeutic purpose).

2. If a dietary supplement is used in a research study, is an IND needed?

According to FDA's 2013 FDA IND Determination Guidance (page 12), whether an IND is needed for a study evaluating a dietary supplement is determined by the intent of the clinical investigation.

- No, an IND is not required if the clinical investigation is intended only to evaluate the dietary supplement's effect on the structure or function of the body or reduce the risk of a disease, intended to support a new or expanded health claim and conducted in healthy individuals over 12 months of age.
- Yes, an IND is required if the clinical investigation is intended to evaluate the dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease. An IND may also be needed if clinical investigations is intended to evaluate whether a food substance/supplement may reduce the risk of a disease in individuals less than 12 months of age, those with altered immune systems, and those with serious or life-threatening medical conditions.

See FDA IND guidance for revised information on which supplement studies require an IND.

Examples of structure/function vs. therapeutic effects:

STRUCTURE/FUNCTION	THERAPEUTIC
Effect on gastric motility	Treatment of constipation
Effect on bone mass	Prevention of osteoporosis
Effect on max O^2 uptake	Improved exercise capacity in heart failure patients

Refer to FDA Guidance Structure/Function Claims, Small Entity Compliance Guide for examples as the distinction between treatment and structure/function effects can be unclear.

3. What options does the IRB or an investigator have if unsure if an IND is needed for a dietary supplement?

A sponsor or sponsor-investigator (S-I) for an investigator-initiated study may make an initial determination regarding the need for an IND and document on the IRB application (Form O). The IRB will review and if unsure may require the S-I to seek an IND determination from FDA. If an FDA determination is required, the S-I may:

- Obtain a written response from FDA that an IND is not needed.
  Submit FDA inquiries to: INDsFoodsDietarySuppCosmetics@fda.hhs.gov
- Submit an IND to the FDA. Provide the IRB with FDA correspondence indicating an IND was not needed or confirming the IND was approved by the FDA.

4. Does an investigator have to include FDA language in the informed consent if conducting a supplement study on structure/function where an IND is not required?

If only evaluating structure or function, FDA does NOT consider a dietary supplement to be a drug.

An investigator would not need to include FDA language in the consent form as long as the study evaluates the supplement's effect on structure or function on the body and not therapeutic effects.

Source: "What is a Drug?" Section of 2013 FDA IND Exempt Guidance

5. Will purchasing the dietary supplement at a health food store exempt the study from IND requrements?

No, if an IND is otherwise required, purchasing the supplement off the shelf does not exempt the study from IND requirements.

6. Does the health status of the study population matter to the IND determination?

   FDA regulations (21 CFR 56.102) define a Human Subject as *"An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient."* An IND may be required in studies including healthy subjects or patients.

   Studies designed to evaluate whether a conventional food or dietary supplement reduces the risk of a disease, effects a structure or function of the body or intended to support a new or expanded health claim, may only be conducted in a population that does not include individuals less than 12 months old, those with altered immune systems, or those with serious or life-threatening medical conditions. Such studies in these vulnerable populations would require an IND.

7. What guidance is available for investigators who have to submit an IND?

   - FDA information for Sponsor-Investigator's submitting an IND http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm071098.htm
   - FDA IND TABLE of links to information for Investigator-Initiated IND Applications http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm343349.htm

8. Does FDA approve dietary supplements for marketing? https://www.fda.gov/food/information-consumers-using-dietary-supplements/questions-and-answers-dietary-supplements

   Unlike drugs, dietary supplements do not undergo a phased FDA approval process before they are marketed. Under DSHEA, FDA requires a manufacturer or distributor only to notify FDA if it intends to market a dietary supplement that contains a "new dietary ingredient" not https://www.fda.gov/food/information-consumers-using-dietary-supplements/questions-and-answers-dietary-supplementsIf the supplement contains a new dietary ingredient, a pre-market review for safety data and other information is required by law. If the supplement does not contain a new dietary ingredient there is no requirement for a manufacturer to provide FDA with the evidence of safety or effectiveness before or after it markets its products.

9. Can a manufacturer market a dietary supplement as a treatment or cure for a specific disease or condition?

   No, a product sold only as a dietary supplement and promoted on its label or in labeling* as a treatment, prevention or cure for a specific disease or condition would be considered an unapproved--and thus illegal--drug. To maintain the product's status as a dietary supplement, the label and labeling must be consistent with the provisions in the Dietary Supplement Health and Education Act (DSHEA) of 1994.

   **Labeling refers to the label as well as accompanying material that is used by a manufacturer to promote and market a specific product.*

Links for Dietary Supplements, Botanicals, Foods, Cosmetics Complementary Medicine Research

- FDA Q & A on Dietary Supplements https://www.fda.gov/food/information-consumers-using-dietary-supplements/questions-and-answers-dietary-supplements
- FDA 101: Dietary Supplements https://www.fda.gov/consumers/consumer-updates/fda-101-dietary-supplements
- FDA Dietary Supplements Website http://www.fda.gov/Food/DietarySupplements/default.htm
- FDA: Is product a cosmetic, drug, or both, or a soap? http://www.fda.gov/cosmetics/guidanceregulation/lawsregulations/ucm074201.htm
- FDA Determining Whether Human Research Studies Can Be Conducted Without an IND - Section V. [republished 10/30/15 with portions related to foods and supplments marked as stayed] http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM229175.pdf
- FDA Stay on Portions of the IND Exempt Guidance (above) relatve to conventional foods and supplements https://www.federalregister.gov/articles/2015/10/30/2015-27729/investigational-new-drug-applications-determining-whether-human-research-studies-can-be-conducted
- FDA FAQ on Botanical Drug Products http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090989.htm
- FDA Complementary and Alternative Medicine Products http://www.fda.gov/RegulatoryInformation/Guidances/ucm144657.htm

- Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues http://www.fda.gov/food/guidanceregulation/guidancedocumentsregulatoryinformation/ucm257563.htm
- Generally Recognized as Safe (GRAS) substance may be added to conventional foods https://www.fda.gov/food/food-ingredients-packaging/generally-recognized-safe-gras
- FDA information for Sponsor-Investigator's submitting an IND http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm071098.htm
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