1. What are dietary supplements?

http://www.fda.gov/Food/DietarySupplements/QADietarySupplements/default.htm#what_is

- 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.
- 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.

Examples of structure/function vs. therapeutic effects:

<table>
<thead>
<tr>
<th>STRUCTURE/FUNCTION</th>
<th>THERAPEUTIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect on gastric motility</td>
<td>Treatment of constipation</td>
</tr>
<tr>
<td>Effect on bone mass</td>
<td>Prevention of osteoporosis</td>
</tr>
<tr>
<td>Effect on max $O_2$ uptake</td>
<td>Improved exercise capacity in heart failure patients</td>
</tr>
</tbody>
</table>

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 SI may:
• Obtain a written response from FDA that an IND is not needed. 

_FDA recommends that the sponsor-investigator contact the appropriate review division (i.e., for the therapeutic area being studied) in the appropriate FDA center for advice about whether the IND regulations apply._

_Organizational charts listing the CBER review divisions and their telephone numbers are available on the Internet at [http://www.fda.gov/AboutFDA/CentersOffices/OrganizationCharts/ucm135943.htm](http://www.fda.gov/AboutFDA/CentersOffices/OrganizationCharts/ucm135943.htm)._ 

• 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. Can the use of a dietary supplement in a research study qualify for an IND exemption of a marketed drug _marketed drug, not intended for reporting to FDA or to changing labeling, no change in dose, population, administration route that significantly increases risk_?

No. The criteria for IND exemption requires that the product be lawfully marketed as an FDA approved drug in the United States. Unless the dietary supplement used in the research study is also a lawfully marketed FDA approved drug, the IND exemption criteria would not apply.

5. 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_

6. Will an IND be needed if you can buy the dietary supplement off the shelf at a health food store?

Yes, if the clinical investigation is intended to evaluate the dietary supplement’s ability to diagnose, cure, mitigate, treat, or prevent a disease, an IND is required. Purchasing the supplement in a health food store does not exempt the study from IND requirements.

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

No. According to FDA Guidance, the clinical condition of study subjects (e.g., the presence or absence of disease) has no bearing on whether the study is subject to the IND requirements. 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.”
8. Does it make a difference to the IND determination if the study information isn’t going to be used for marketing?

No. Whether the intent of the clinical investigation is commercial or noncommercial is not a factor in the IND determination.

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

- FDA information for Sponsor-Investigator’s submitting an IND

- FDA IND TABLE of links to information for Investigator-Initiated IND Applications

10. Does FDA approve dietary supplements for marketing?

http://www.fda.gov/Food/DietarySupplements/QADietarySupplements/default.htm#what_is

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 currently sold in a dietary supplement, in the U.S. before October 15, 1994.

If 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.

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

No, a product sold 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 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.

• FDA FAQ on Botanical Drug Products
  http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090989.htm

• FDA Q and A on Dietary Supplements
  http://www.fda.gov/Food/DietarySupplements/QADietarySupplements/default.htm

• FDA Complementary and Alternative Medicine Products
  http://www.fda.gov/RegulatoryInformation/Guidances/ucm144657.htm

• New Dietary Ingredients in Dietary Supplements www.fda.gov/Food/DietarySupplements/ucm109764.htm

• Draft Guidance for Industry: Dietary Supplements: New Dietary Ingredient Notifications and Related Issues
  http://www.fda.gov/food/guidanceregulation/guidancedocumentsregulatoryinformation/ucm257563.htm

• Medical Foods FAQ - under MD supervision (e.g., for inborn error of metabolism – reduced phenylalanine for PKU)
  www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/MedicalFoods/ucm054048.htm

• 2013 FDA Determining Whether Human Research Studies Can Be Conducted Without an IND

• 2004 FDA Guidance on IND exemptions for marketed products in cancer treatment

• FDA information for Sponsor-Investigator’s submitting an IND

• FDA IND TABLE of links to information for Investigator-Initiated IND Applications