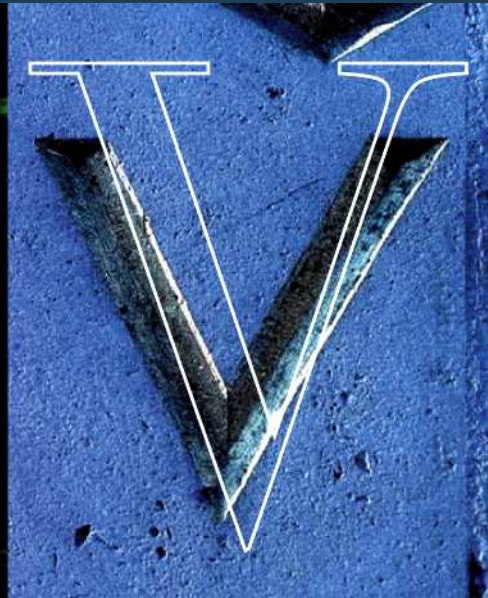
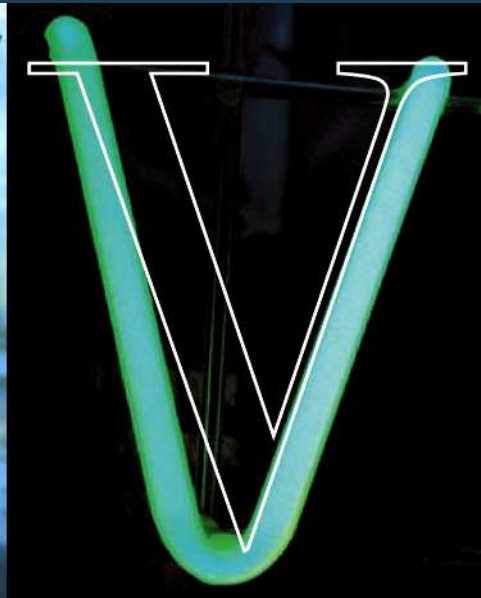
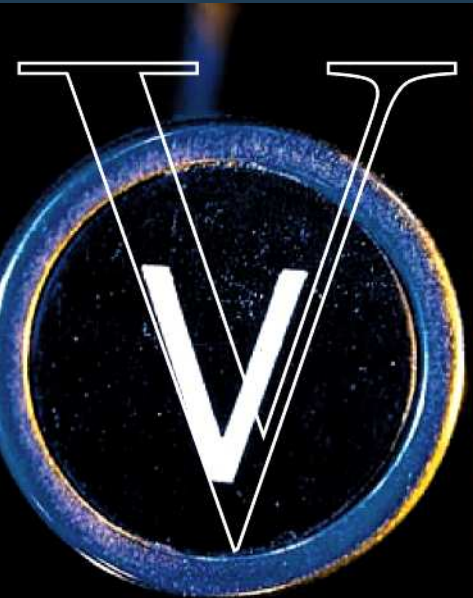
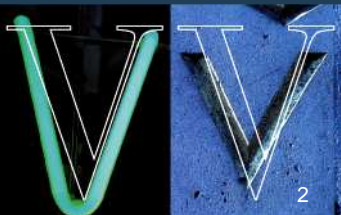


VENABLE[®]_{LLP}

Pathway to Market – Medical Food, Dietary Supplement, or Drug

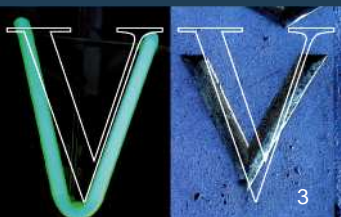


Key Definitions



Definition of a Medical Food

- A Medical Food is defined as a food
 - formulated to be consumed or administered enterally under the supervision of a physician,
 - that is intended for the specific dietary management of a disease or condition,
 - for which distinctive nutritional requirements, based on recognized scientific principles, have been established by medical evaluation
- Narrowly construed
 - FDA warning letters have indicated that allergies, arthritis, asthma, cardiovascular disease, fibromyalgia, chronic fatigue syndrome, failure to thrive, prenatal vitamins, autoimmune disorders, and diabetes are not conditions with distinctive nutritional requirements



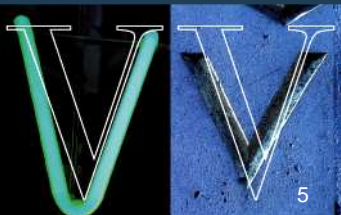
Definition of a Dietary Supplement

A dietary supplement is defined as a product:

- that is intended to supplement the diet, which contains one or more of the following dietary ingredients: a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combination of these ingredients.
- ingested in pill, capsule, tablet, or liquid form.
- not represented for use as a conventional food or as the sole item of a meal or diet.

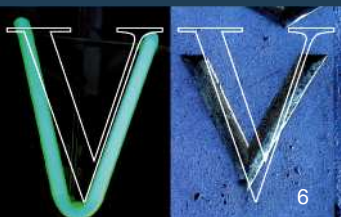


Key Requirements for Medical Foods



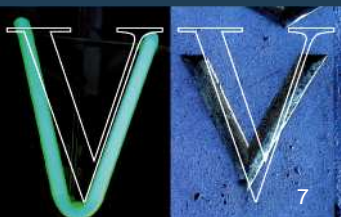
Specifically Formulated and Processed

- A medical food is specially formulated and processed (as opposed to a naturally-occurring food used in its natural state) for the partial or exclusive feeding of a patient by oral intake or tube.



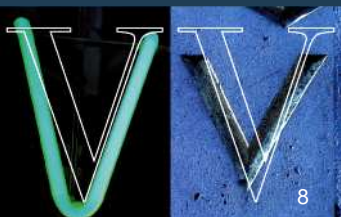
Dietary Management of a Patient

- Medical food is intended for the dietary management of a patient who has
 - limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs or certain nutrients because of therapeutic or chronic medical needs, or
 - other special medically-determined nutrient requirements that cannot be addressed through modification of the normal diet alone
 - **Ganeden Biotech 2006 Warning Letter** – Psoriasis, chronic constipation, arthritis, Crohn’s Disease and Colitis, and IBS do not have distinct nutrient requirements
 - **Medical Food Draft Guidance (August 2013)** – Type 1 and Type 2 Diabetes Mellitus (DM) are not conditions for which a medical food can be labeled and marketed. *[[“Diet therapy is the mainstay of diabetes management. A regular diet can be modified to meet the needs of an individual affected by either type of DM.”]]*



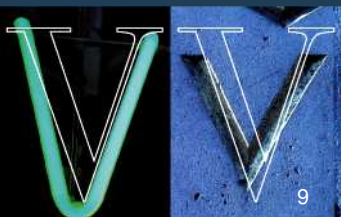
Unique Nutritional Requirements

- Medical foods provide nutritional support specifically modified for the management of the unique nutrient needs that result from a specific disease or condition, as determined by medical evaluation
 - **Accera, Inc. Warning Letter 2013** – No distinctive nutritional requirements or unique nutrient needs for individuals with mild to moderate Alzheimer’s disease.
 - **Bioenergy Corvalen Warning Letter 2010** – No distinctive nutrient need for patients with fibromyalgia, chronic fatigue syndrome, or cardiovascular disease
 - **Nestle’s Boost Kid Essential Warning Letter 2009** – No distinctive nutrient need for the medical condition “failure to thrive”
 - **Efficas Warning Letter 2007** – No distinctive nutrient need for individuals suffering from allergies or asthma
 - **Metagenics Warning Letter 2003** – No distinctive nutrient requirements for type 2 diabetes, arthritis, psoriasis, eczema, chronic fatigue, and migraine headaches.

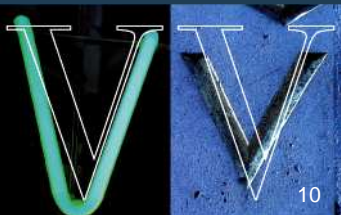


Medical Supervision

- It is intended for use under medical supervision.
 - HOWEVER, the August 2013 Draft Guidance makes it clear that medical foods do *not* have to be prescribed. As a result, medical foods may note have an “Rx only” symbol.
- Medical foods are intended only for patients receiving active and ongoing medical supervision, wherein the patient requires medical care on a recurring basis for, among other things, instructions on the use of the medical food.



Path to Market for Medical Foods



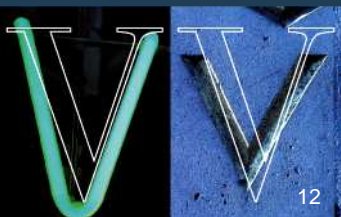
Barrier of Entry is Moderate

- Does not require FDA approval, but
 - FDA views this category as being very narrow
 - FDA will require all ingredients to be GRAS-E
 - The minimum efficacy requirement is the Significant Scientific Agreement (SSA) standard
 - Distribution Channels are limited
 - Importing, without prior, consultation with FDA, is done at the company's own peril
 - FDA may not believe a pill is an appropriate delivery vehicle.



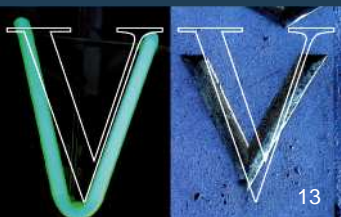
Unique Nutritional Need Requirement

- Scientific dossier must be developed to demonstrate that a specific disease or medical condition has unique nutritional needs that cannot be otherwise met through modification of the diet alone.
- The nutritional need requirement will require at a minimum Significant Scientific Agreement.
 - It is insufficient to state the product works nutritionally if the scientific literature does not show that the nutrients you are providing *are necessary*.
 - Cannot use the Medical Food category to circumvent the New Drug Approval process.



SAFETY

- Medical foods, like “conventional” food products, must contain only ingredients that are either GRAS for use in food or approved as food additives by FDA.
 - The ingredients must be generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of intended use.
 - May require at least one safety study in the intended patient population.



Medical Food - Effectiveness

- At a minimum, FDA would require Significant Scientific Agreement to establish the effectiveness of a medical food.
 - In an advanced notice of proposed rulemaking (withdrawn), FDA indicated that the scientific evidence is likely somewhere between the SSA standard and the standard for a new drug approval.
 - The FDA has indicated its position on this issue by stating, “it is essential that the claims made for such a product present an accurate interpretation of the scientific evidence concerning the usefulness of that product or specific formulation..., [and]...a strong standard of substantiation would be one that requires that all pertinent data be considered in the formulation of the product and in the development of any claims about its use.” FDA Advanced Notice of Proposed Rulemaking, 61 Fed. Reg. 60661, 60669-70 (Nov. 29, 1996).



Marketing Channel

- The Orphan Drug Act does not restrict the marketing channel that Medical Foods may be marketed.
 - FDA takes a limited view of the marketing channel
 - Hospitals, pharmacies (behind the counter), and physician offices, etc.
 - FDA does not believe that the products should be mass marketed
 - Are Glucerna and Boost Glucose Control medical foods, foods for special dietary use, or hybrids?
 - » Labeled to be taken under the supervision of a medical practitioner
 - » Mass marketed
 - » Dietary uniqueness



Examples of Medical Foods Presently Marketed

- Axona[®] - A prescription medical food that is marketed for the dietary management of Alzheimer's. **[[Accera received a warning letter in December 2013 that stated Axona is not a medical food because there are no distinctive nutritional requirements or unique nutrient needs for individuals with mild to moderate Alzheimer's]].**
- GlycemX[™] 360 – A medical food that is marketed for the dietary management of diabetes. **[[Metagenics received a warning letter in August 2013 that stated GlycemX is intended to support a condition (Diabetes Mellitus) that does not have distinct nutritional requirements]].**
- VSL#3[®] - A probiotic medical food marketed for the treatment of IBS, ulcerative colitis, etc.
- Limbrel[®]500 – A medical food marketed for the treatment of osteoarthritis.



Dietary Supplement Core Concepts



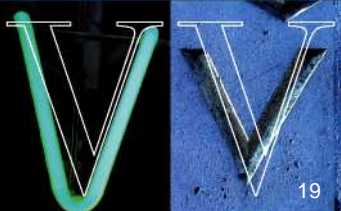
SAFETY

- Under DSHEA, a supplement or dietary ingredient is unsafe if:
 - It presents a significant or unreasonable risk of illness or injury, under the conditions of use recommended or suggested in labeling, or under ordinary conditions of use, or
 - It is a new dietary ingredient (NDI) for which there is inadequate information to provide assurance that it does not present a significant or unreasonable risk of illness or injury.



New Dietary Ingredients

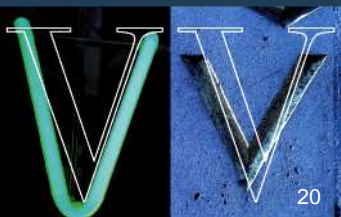
A “new dietary ingredient” is an ingredient that was not marketed in the United States before October 15, 1994, and does not include any dietary ingredient which was marketed in the United States before October 15, 1994.



New Dietary Ingredients

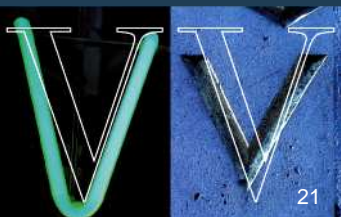
Questions & Answers About NDIs

- Q1:** What if I know that an ingredient was marketed before October 15, 1994, but do not have evidence? Must I submit an NDI notification?
- Q2:** My ingredient is an extract of a food that was present in the food supply before October 15, 1994. Do I need to submit an NDI notification?
- Q3:** My ingredient was a component of food in the food supply in chemically altered form. Do I need a NDI notification?



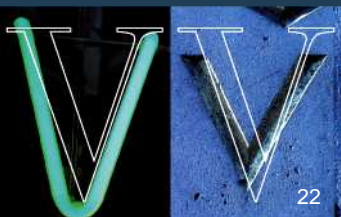
Dietary Supplement Claims

- Health Claims
- Qualified Health Claims
- Nutrient Content Claims
- Structure / Function Claims



Dietary Supplement Claims: 30-Day Notification

No more than thirty (30) days after a supplement bearing a structure/function claim is marketed, the manufacturer, packer, or distributor of the supplement must notify the FDA Office of Nutritional Products, Labeling and Dietary Supplements.



Dietary Supplement Claims: Disclaimer

The FD&C Act requires the following disclaimer to appear in connection with a structure/function claim:

“This/these claim(s) has/have not been evaluated by the Food and Drug Administration . This product is not intended to diagnose, treat, cure or prevent any disease.”

Statement must also...

- ✓ Be at least 6 point font size,
- ✓ Be bold,
- ✓ Be entirely enclosed inside a box,
- ✓ Be listed by itself preferably on the same panel as claim or include a link to the claim.



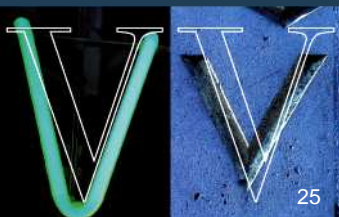
Dietary Supplement Claims: Substantiation

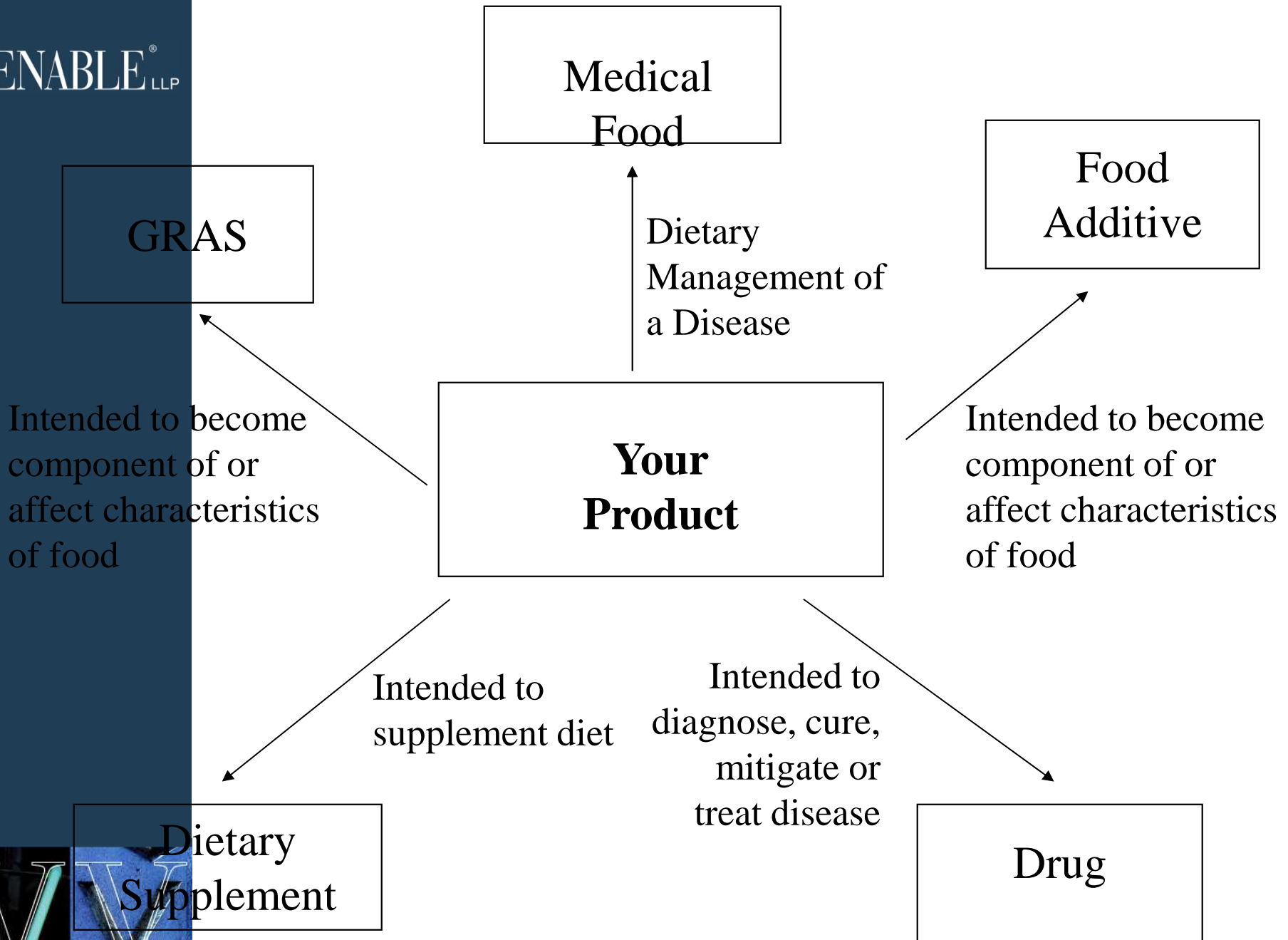
In considering the number and type of studies required to substantiate a claim, advertisers should consider:

1. The meaning(s) of the claims being made, express and implied;
2. The relationship of the evidence to the claim;
3. The quality of the evidence; and
4. The totality of the evidence.
5. Accepted norms in the relevant research field.



Drug, Medical Food, or Dietary Supplement: The Pros and Cons of Each Approach

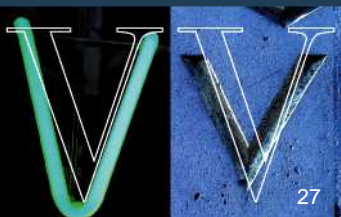




Drug Pro's

Pro's of marketing drugs that have gone through FDA's approval process

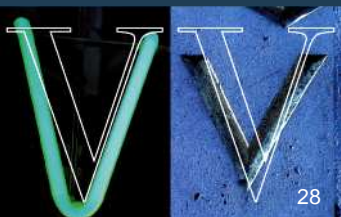
- Make express disease claims
- Exclusivity during initial marketing phase regardless of patent consideration
- Higher price point
- Prescription drugs covered by insurance plans



Drug Con's

Cons of marketing drugs that have gone through FDA's approval process

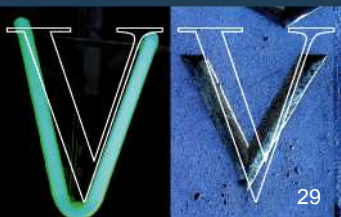
- Extensive amount of R&D time
- Drug approval process takes years
- Costs will most likely be in the tens of millions, if not higher
- No guarantee of approval
- Significant regulatory oversight



Medical Food Pros

Pro's of marketing a product as a medical food

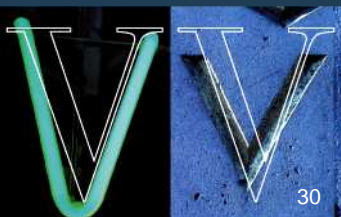
- Lower barrier to market entry
- FDA premarket approval not required
- Express disease management claims
- Less costly to manufacture
- Less regulatory oversight
- FDA objects may be able to rebrand as a dietary supplement or conventional food with appropriate structure/function claims



Medical Foods Con's

Cons of marketing products as a medical food

- Extensive amount of R&D time
- Requires at least Significant Scientific Agreement
- Clinical studies are costly
- Category narrowly construed
- Limited marketing channels
- Lower barrier of entry
- FDA may disagree that the product is appropriately marketed as a medical food



Dietary Supplement Pro's

Pro's of marketing an ingredient as a food or dietary supplement

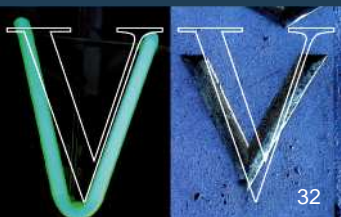
- Lowest barrier to market entry
- No FDA premarket approval required – NDI is a notification, not an approval process – Interesting issue whether FDA can deny a notification
- No restrictions on marketing channels
- U.S. consumers understand the implied meaning of structure/function claims
- Less costly to manufacture
- Less regulatory oversight



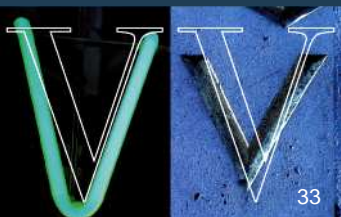
Dietary Supplement Con's

Con's of marketing an ingredient as a food or dietary supplement

- Limited to structure/function claims or FDA-permitted health claims
- Generally not covered by insurance
- Generally no barriers to entry by competitors



Questions?



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