Selling The Science:
The Fine Print on Bioavailable Claims

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FDA Considerations

Was your ingredient an Old Dietary Ingredient (ODI)?

Increased bioavailability may be a manufacturing change, making the product no longer an “ODI.”

ODI "Manufacturing Changes"

12. If I change the manufacturing process for a dietary ingredient that was marketed in the U.S. prior to October 15, 1994, does that make the ingredient an NDI?

Any changes in your manufacturing process that alter the identity of the ingredient will convert a previously marketed dietary ingredient into an NDI. Manufacturing changes that alter the physicochemical structure or properties, purity and impurities, or biological properties (such as bioavailability or toxicity) of the ingredient result in an NDI.[18] For example, using a solvent to prepare an extract from a pre-DSHEA

Dietary Supplements: New Dietary Ingredient Notifications and Related Issues: Guidance for Industry

ODI “Manufacturing Changes”

“Alterations in the physical and chemical properties of a food substance can affect its bioavailability through altered absorption, distribution, metabolism and excretion of the substance in the body. Such changes in the substance’s biological interactions can affect the level at which toxic effects may occur.”

Guidance for Industry Assessing the Effects of Significant Manufacturing Process Changes, Including Emerging Technologies, on the Safety and Regulatory Status of Food Ingredients and Food Contact Substances, Including Food Ingredients that are Color Additives

NDI “Chemical Alterations”

New Dietary Ingredients (NDIs) are required to submit a New Dietary Ingredient Notification, unless…

“The dietary supplement contains only dietary ingredients which have been present in the food supply as an article used for food in a form in which the food has not been chemically altered.”

21 U.S.C. § 350b(a)(1)

NDI “Chemical Alterations”

There is a very narrow definition of what is *not* a chemical alteration.

- Physical modifications are generally not chemical alterations
  - “Minor loss of volatile components, dehydration, lyoph[i]lization, milling, tincture or solution in water, slurry, a powder, or solid in suspension”

- Mostly everything else will be a “chemical alteration.”
  - E.g., processes that make/break chemical bonds, nanotechnology

FDA Considerations

Bottom line: the regulatory classification is likely impacted.

- If you were relying on ODI status → shift to think in the NDI context
- If you were relying on a food supply exemption → reanalyze

That said, the adulteration standard still applies

- These standards consider manufacturing of the dietary ingredient itself
  - Some methods don't change the ingredient, like other absorption enhancing ingredients, and therefore ODI/NDI status is not impacted
- But the product must still be safe for consumption
  - FDA's NDIN guidance states the safety narrative still should address the "bioavailability of the ingredients as formulated"

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BBB National Programs
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You Get a Claim! And You Get a Claim!

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"Bioavailable Form"

"10x More Bioavailable Than Standard XX"

"Clinically Proven Bioavailability"

"Superior Bioavailability"

"Absorbed 20x faster than regular XX"

"Delivers More Than Standard Capsules"

Substantiate That Claim

- All claims must be truthful, not misleading, and adequately substantiated.
  - Health claims must be supported by “competent and reliable scientific evidence” (CARSE)

- To be CARSE, a study establishing bioavailability generally must:
  - Be in humans
  - Placebo-controlled
  - Using the same dosage
  - Following the directions for use
  - Statistically significant results between groups
  - Clinically meaningful results

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The Claim Type Affects Substantiation

- Monadic claims
  - Generally fine with product only study

- Comparative claims
  - Require head-to-head product testing
    - Must follow both product's directions verbatim
    - Avoid conditions that are favorable to one over the other
      - E.g., feeding with a meal or taking with water
  - Broad claims that do not identify a specific comparator must be true compared to the top 85% of the marketplace
    - Based on sales volume (usually units)

Context Matters

Be careful expressly or impliedly tying bioavailability to health outcomes!

Can imply greater efficacy or benefits, which changes the substantiation burden.

"Superior Bioavailability for Heart Health"

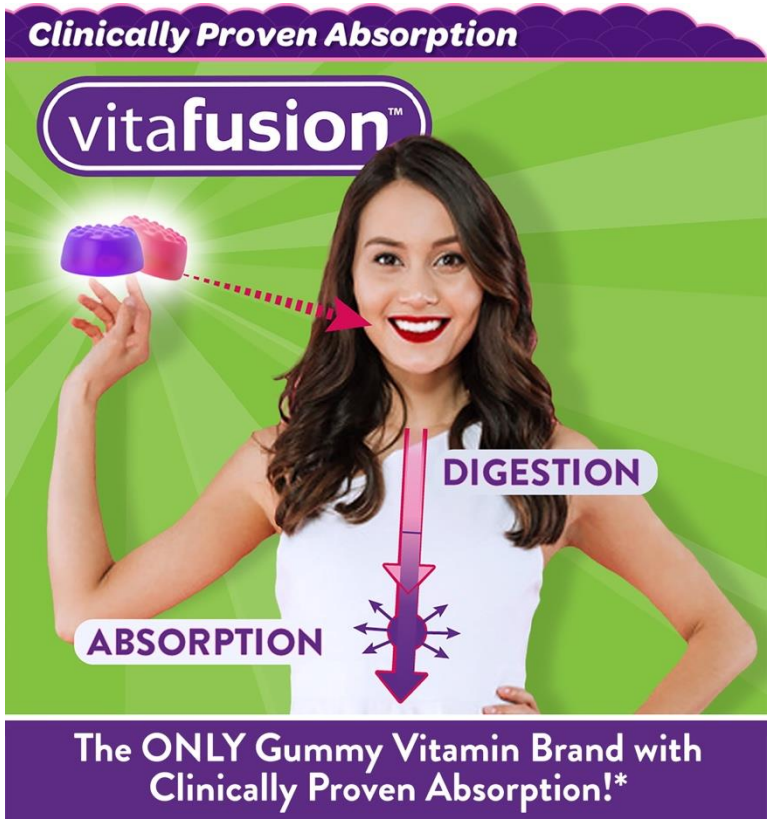
vs.

"Superior Bioavailability"

"For Heart Health"

Case Study – “Clinically Proven Absorption”

- Four studies:
  - An acute, high-dose, single-nutrient formulation of Vitamin C
  - Two acute, high-dose, single-nutrient formulation of Vitamin D3
  - One acute, high-dose multivitamin study measuring Vitamin C & D3
- All crossover, randomized, comparator-controlled studies
- All dosages exceed the products in market
  - 1000mg Vitamin C tested vs. 240mg or between 6-90mg
  - 20,000 IU Vitamin D3 tested vs. 3,000 IU or between 200-2,000IU



Case Study – "Clinically Proven Absorption"

NAD found the claim was not adequately substantiated!

- Rejected that such practice was standard, and that it was necessary to overcome "noise" from confounding consumption
  - Persuaded by possible alternative methods raised by challenger
- Rejected expert report on:
  - The dosage discrepancy & extrapolating downward based on the known mechanism of action
- Significant concern with "proven" claim, which reasonably implied clinical proof of absorption in consumer meaningful amounts
  - This couldn't be bridged with the mega-doses

Church & Dwight Co., Inc. (Vitafusion Gummy Vitamins), Report #6355, *NAD/CARU Case Reports* (March 16, 2020).

Advertising Checklist

- What support do I have for the claim?
  - Any weaknesses or shortcomings that increase risk?
- Is my claim tailored to the support I have?
  - Is it overly broad or include on products with different formulations?
- Is there any context around my claim that may change its meaning?
  - Advertisers are responsible for all reasonably implied claims, even if not intended.

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Thank You!

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