



BACKGROUND

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FDA Draft Guidance on New Dietary Ingredients for the Dietary Supplement Industry

What is a New Dietary Ingredient?

When Congress enacted the Dietary Supplement Health and Education Act (DSHEA) in 1994, it created two kinds of dietary ingredients for use in supplements: old (“grandfathered”) ingredients that were already being sold prior to the enactment of DSHEA and new dietary ingredients (NDIs) not marketed in the United States before October 15, 1994, ten days prior to enactment of DSHEA. Dietary ingredients already in commerce before the “grandfathered” date were considered by Congress to be safe unless FDA demonstrated they were not. FDA has the burden to show that a “grandfathered” ingredient presents a “significant or unreasonable risk of injury or illness” to remove a dietary supplement from the market. For new dietary ingredients, DSHEA requires a premarket notification to FDA at least 75 days before a new ingredient is placed into commerce unless the ingredient is a constituent of a food and has not been chemically altered. The manufacturer must provide in that notification either a history of use or other evidence that the ingredient is “reasonably expected to be safe.” See *section 413(c) of the Federal Food, Drug and Cosmetic Act (FDCA)*.

Overview of NDIs and DSHEA:

Over the past seventeen years, the industry and FDA seem to have developed very different views of when an NDI notification is required and what data should be presented to FDA to satisfy the “reasonably expected to be safe” standard. Until now, FDA had not provided any guidance to manufacturers on what should be provided in an NDI notification except for what companies could glean from the experiences of other manufacturers. During that time, FDA objected to more than 450 notices, while only acknowledging (i.e., not objecting to) 162 notifications. In 1997, FDA issued a regulation on the NDI notification process that largely reiterates the statutory requirements but offered little clarity of FDA’s interpretation. Despite the Agency’s criticism that the industry was filing far too few NDI notifications, FDA has only issued one warning letter to a firm for failing to file the required paperwork. Clearly, there is confusion as to when an NDI notification should be submitted and what should be included in the notification.

Against this backdrop, the dietary supplement industry began pressing for a guidance to clarify NDI notification requirements. Finally, at the insistence of Congress in the Food Safety Modernization Act (P.L. 111-353), FDA issued a draft *Guidance for Industry: New Dietary Ingredient Notifications and Related Issues* in July 2011. Industry believes that FDA’s current interpretation has disregarded Congress’ original intent for NDIs. The release of the draft NDI notification guidance raises fundamental questions for the implementation of DSHEA.

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In the early 1990s, FDA attempted to regulate dietary ingredients as unapproved new food additives, thereby imposing on particular dietary ingredients the same requirements for premarket approval as it applied to chemicals that were added to food for non-nutritive reasons. The court struck down that effort accusing FDA of trying to make an end-run around the statutory scheme (e.g., the black currant oil cases).

In 1994, Congress enacted DSHEA stating that dietary supplements shall not be regulated as food additives or as drugs. DSHEA specified the types of ingredients that were to be permitted in dietary supplements and authorized statements of nutritional support describing how a product affects the structure and function of the body. Since passage, it has been successful in providing consumers with a broad range of safe and beneficial products. However, with the new draft NDI guidance, it would appear that FDA is attempting to revive the “food additive” approach to regulating dietary supplements.

Draft NDI Guidance Raises Fundamental Concerns for Implementation of DSHEA

The following items included in the July 2011 draft guidance are particularly concerning:

- FDA does not consider synthetic versions of botanical ingredients to be legitimate dietary ingredients. Even though the ingredient is bio-identical to its botanical counterpart, FDA states that it was “never part of the botanical” so it cannot be characterized as a constituent. Note this is not an issue of the safety of the ingredient; manufacturers use bio-identical synthetics because they are more uniform, more environmentally sustainable and more commercially viable than harvesting the plant.
- FDA places the burden to prove an ingredient is “grandfathered” onto the marketer. FDA rejects industry-prepared lists of pre-1994 ingredients and affidavits of manufacturers as evidence of pre-1994 sales, saying marketers must prove to FDA with documentary evidence that the ingredient was marketed prior to 1994. That makes it difficult to prove old ingredient status and allows FDA to re-characterize many old ingredients as new ones. Also, newer companies would be disadvantaged if they are not able to demonstrate a pre-1994 sale of an ingredient by another manufacturer.
- While the law is clear that an old ingredient that is “chemically altered” becomes a new ingredient, FDA broadly defines what is “chemically altered” so that changes in extraction methods and other innovations since 1994 may make “grandfathered” ingredients – long presumed to be safe – into new ones, subject to additional, burdensome scientific assessment. This would likely result in a backlog of notifications for industry and FDA alike if all these ingredients required NDI filings and constrain innovation while increasing the costs to bring new technology to market.
- FDA interprets the statute to require that every product that contains an NDI would require a separate notice to FDA with a separate demonstration of safety. DSHEA says the ingredient must “reasonably be expected to be safe,” but FDA wants each finished product containing the NDI to have its own notification on file. Under FDA’s view, ingredient

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suppliers would not be able to “do the science” for their customers, as each formulation would need a separate NDI notice. This could result in redundant notifications for similar products, creating increased costs to industry and more backlog at FDA.

- Finally, FDA describes in the draft guidance what it views as the necessary level of science to prove a reasonable expectation of safety, which is well beyond what is included in statute. And it resembles the science required for a food additive petition – the standard Congress and the courts rejected nearly 20 years ago! Consider that the draft guidance repeatedly references the *Redbook (Toxicological Principles for the Safety Assessment of Food Ingredients)* as authoritative for demonstrating the safety of dietary ingredients. The Redbook is the official textbook for evaluating food additives at the significantly higher threshold than the reasonably expected to be safe standard Congress prescribed for new dietary ingredients.

Collectively, the draft NDI guidance can be viewed as a variety of maneuvers by FDA to re-characterize as many dietary ingredients as possible as NDIs, and then to impose a standard of proof for their safety that few manufacturers would be able to meet; one that Congress and the courts clearly did not intend to be applied to dietary supplements.

If the guidance were enforced, it could restrict innovation and product improvements, and would likely overwhelm FDA with submissions as responsible industry begins to comply with the guidance’s more onerous demands. With limited federal funds, there are concerns that FDA may inappropriately use its scarce resources to enforce this guidance, instead of focusing on egregious actors who are illicitly engaged in defrauding the consumer by spiking dietary supplements with illegal prescription drugs and anabolic steroids. But what is certain is that the economic impact of this draft guidance on the dietary supplement industry would be substantial (i.e., loss of jobs, availability of products, restricted access).

What Happens Next?

Because the July 2011 guidance continues to be in draft form, CRN remains hopeful that FDA will listen carefully to industry’s comments and will be open to significant modifications. CRN filed thoughtful and extensive comments that elaborate how the draft guidance misreads the statute, misinterprets the legislative history of DSHEA, and ignores the precedent of 17 years of FDA’s implementation of the NDI requirements.

CRN is concerned that FDA has tried to redistribute the respective burdens of proof for demonstrating the safety of dietary ingredients in ways that DSHEA never intended.