



Dietary Supplements: What Are They and How Are They Regulated?

Overview

More than half of American adults take at least one dietary supplement a day.¹ And the number of these products on the market is growing—from about 4,000 in 1994 to about 80,000 today, for an estimated \$40 billion in sales.² With such widespread use of supplements, consumers need to be confident about their quality and safety.

What is a dietary supplement?

According to the Dietary Supplement Health and Education Act (DSHEA) of 1994, a dietary supplement contains one or more vitamins, minerals, herbs or other botanicals, amino acids, or other dietary ingredients; is intended to be taken by mouth as a pill, capsule, tablet, powder, or liquid; and is identified as such on the label.³ Supplements range from children's vitamins to weight-loss and sports nutritional products marketed to adults. According to "Dietary Guidelines for Americans," a 2015 report issued by the departments of Agriculture and Health and Human Services, taking one or more dietary supplements may be beneficial when a person does not get the recommended amount of nutrients from foods. Examples of such nutrients are vitamin D for adults and children with limited sunlight exposure, and iron and folic acid for women who are pregnant or capable of becoming pregnant.⁴ However, many dietary supplements are not essential nutrients and have no proven medical benefits.

How are dietary supplements regulated?

The DSHEA established that dietary supplements are a category of food and therefore are regulated as such—not as drugs. This means that manufacturers do not need to prove that dietary supplements are safe and effective before they can market them.

Supplement manufacturers also do not need to notify the Food and Drug Administration that a new product is on the market unless they intend to make a structure/function claim about it⁵ (described below) or unless the product contains a new dietary ingredient (NDI)—such as a vitamin, mineral, or herb that was not on the U.S. market before Oct. 15, 1994.⁶ If a supplement contains an NDI, the manufacturer must send FDA a notification at least 75 days before it is introduced, demonstrating a history of use or other evidence that the ingredient “will be reasonably expected to be safe.” Supplements that contain only dietary ingredients that have been present in the food supply and have not been chemically altered are exempt from this requirement.⁷

If a manufacturer or distributor fails to submit an NDI notification when one is warranted, or if FDA determines that there is insufficient history of use or evidence that the NDI can reasonably be expected to be safe, the supplement will be deemed adulterated.⁸ Supplements are also considered adulterated if they present a significant or unreasonable risk of illness or injury under their recommended use, the label’s indication, or ordinary conditions of use; if they pose an imminent hazard to public health or safety; or if the supplement has been prepared, packed, or held under conditions that do not meet current manufacturing regulations.⁹

Dietary supplements are considered misbranded foods if the labeling is false or misleading.¹⁰ Specific misbranding provisions apply if the label fails to list each ingredient’s name and quantity; identify the product as a dietary supplement; or (if the dietary ingredient is an herb or botanical) state from which plant an ingredient is derived.¹¹

If FDA deems a dietary supplement to be adulterated or misbranded, the agency is responsible for taking action. It may take administrative action by issuing a mandatory recall, suspending a manufacturer’s registration, detaining a product identified during an inspection, or blocking an imported product’s entry.¹² Or it may also take judicial action, by, for example, seeking an injunction against a manufacturer, prosecuting a manufacturer, or filing a seizure action against products that are adulterated, misbranded, or otherwise in violation of federal law.¹³ In some cases, FDA may conduct rule-making to restrict or prohibit the use of a specific ingredient.¹⁴ In any case, the agency must demonstrate that the relevant statutory standard has been met.¹⁵ For example, before FDA can take action against a firm manufacturing an adulterated dietary supplement, it must demonstrate that it presents a “significant or unreasonable risk of illness or injury.”¹⁶

What claims can supplements make?

Dietary supplement advertising and labeling may include statements or claims about the product’s ingredients and their benefits. Manufacturers are responsible for ensuring that any dietary supplement claims are truthful and not misleading, and FDA and the Federal Trade Commission (in the case of advertising) have authority to review those claims to determine whether they meet statutory requirements.

Marketing for dietary supplements cannot claim that the supplement will diagnose, treat, cure, or prevent any disease; products that include such “disease claims” are regulated as drugs. Supplement manufacturers can, however, make four types of claims:

1. **Structure/function claims** describe the effect of a dietary ingredient on the structure or function of the body or characterize the actions by which the ingredient maintains such structure or function. Examples include “calcium builds strong bones” or “fiber maintains bowel regularity.” FDA does not need to preapprove or

review the scientific basis of such claims, but manufacturers must have substantiation to support them and submit the claim to FDA no later than 30 days after the product is first marketed.¹⁷

2. **Health claims** describe the relationship between a dietary ingredient and disease or other health-related condition. These claims require FDA authorization and are contingent upon the agency's review of the evidence and determination that there is "significant scientific agreement" to support the claim.¹⁸ An example of a codified health claim is "Adequate calcium and vitamin D throughout life, as part of a well-balanced diet, may reduce the risk of osteoporosis."¹⁹
3. **Qualified health claims** allow manufacturers to make health claims based on less evidence than the significant scientific agreement standard. Manufacturers must petition FDA, which determines whether the claim misleads consumers.²⁰ An example of a qualified health claim is, "Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease. One serving of [Name of the food] provides [] gram of EPA and DHA omega-3 fatty acids. [See nutrition information for total fat, saturated fat, and cholesterol content.]"²¹
4. **Nutrient content claims** characterize the level of a nutrient in a product and are limited to those authorized by FDA regulation.²² Examples of such claims include "sugar free" or "high in vitamin C."

How are quality and safety ensured?

The degree of quality control for dietary supplements depends on the ingredient suppliers, manufacturers, and others in the production process. In 2007, FDA issued a final rule establishing current good manufacturing practices (cGMPs) for dietary supplements. Manufacturers must ensure that the identity, purity, strength, and composition of a dietary supplement product are accurate. The regulation requires manufacturers to establish procedures for quality control, laboratory testing, and other operations.²³ These procedures help prevent the wrong ingredients from being used in supplements, ensure the appropriate amount of an ingredient, protect against contamination by substances such as lead or banned pharmaceuticals, and avoid improper packaging and labeling. If dietary supplements contain contaminants or have an ingredient not listed on the label, FDA considers those products to be adulterated or misbranded, respectively.

Although FDA inspects registered dietary supplement manufacturers—and unregistered facilities when it becomes aware of them—the agency is able to visit only a small fraction of facilities because of resource limitations, and not every entity selling dietary supplements is registered with FDA. Moreover, facility registrations are renewed on a biennial basis,²⁴ so FDA does not always have the most current information. Even when manufacturers register their facilities, they do not have to tell FDA what they are making, compromising the agency's ability to prioritize inspections based on risk. In part because of resource constraints, FDA cannot routinely track compliance with cGMP regulations, but even its limited number of inspections has revealed quality and safety concerns. In 2015, the agency reported that it inspected about 500 of nearly 13,000 registered facilities and found violations in almost 300 of them.²⁵

Consumer Harm Associated With Adulterated Dietary Supplements

When dietary supplements manufacturers sell adulterated or misbranded products, intentionally or because they do not have effective systems to prevent errors, consumers can be harmed. For example, in 2016, FDA discovered lead in Life Rising's DHZC-2²⁶ product, marketed for regulating blood circulation, after the agency received an adverse event report. FDA notified the company about its findings, and the firm voluntarily recalled the product. After the initial recall, FDA learned of five adverse events possibly associated with DHZC-2 tablets, three of which involved children who may have consumed the tablets and who were found to have elevated lead levels in their blood. Exposure to lead in childhood can cause learning disabilities, developmental delays, and lower IQ scores.²⁷

Another adulterated dietary supplement that caused adverse events is OxyElite Pro, a weight loss product. In September 2013, FDA learned of an acute outbreak of nonviral hepatitis in Hawaii.²⁸ An investigation by the Centers for Disease Control and Prevention and the Hawaii Department of Health revealed that seven patients had used the product. FDA also identified patients outside Hawaii who had similar liver dysfunction after using OxyElite Pro. The next month, FDA notified the public of the potential link between OxyElite Pro and acute liver failure. The agency also issued a warning letter to USPlabs, the product's manufacturer, stating that OxyElite Pro was adulterated because it contained a new dietary ingredient for which the company had not provided evidence of safety.²⁹ FDA ultimately found that 27 patients in Hawaii had taken the product and that 17 of them had reported that OxyElite Pro was the only dietary supplement they were taking. One of these patients died, another patient required a liver transplant, and others await liver transplants.³⁰ In November 2013, FDA sent a second letter to USPlabs notifying it that OxyElite Pro had been linked to liver illnesses and threatening to halt the supplement's distribution and sales if the company did not initiate a voluntary recall. USPlabs recalled its product days after receiving the letter.³¹ Two years later, the Department of Justice, FDA, and other federal agencies brought criminal charges against USPlabs.³²

How does FDA identify and resolve safety problems?

Because FDA generally does not have premarket review authority over dietary supplements, it must rely on postmarket surveillance methods to identify potential safety problems. When a consumer is harmed by a supplement, manufacturers, consumers, and health care providers can report the case directly to FDA through the Safety Reporting Portal.³³ In addition, manufacturers are required to notify FDA of serious adverse events related to use of their dietary supplement products.³⁴ A 2015 study estimated that such events are responsible for 23,005 emergency room visits a year. The researchers concluded that the actual number is probably larger because of underreporting by patients and physicians who do not readily associate adverse events with dietary supplement use.³⁵

Once FDA is made aware of a safety concern, the agency must prove that the dietary supplement presents a risk before it can take enforcement actions.³⁶ FDA may issue a warning letter to give a manufacturer a chance to remedy the violation before initiation of an enforcement action. If the manufacturer does not take adequate

corrective actions, the agency can consider further administrative or regulatory action, such as a mandatory recall.³⁷ To remove a supplement from the market, FDA must demonstrate that the product is adulterated or misbranded and that use or exposure to it will cause injury or death. The agency must then give the manufacturer a chance to recall the product.³⁸ If the manufacturer does not cease distribution or issue a recall, FDA can mandate that it cease distribution and notify its customers.³⁹ However, underreporting of adverse events involving consumers, inadequate supply-chain record keeping, and limited facility inspections hinder FDA from more effectively asserting its authority to ensure the safety of dietary supplements.

Recalls initiated by the manufacturer, by FDA request, or by FDA order under statutory authority may also be used to remove dietary supplements that contain active pharmaceutical ingredients (API) from the market.⁴⁰ Class I recalls are reserved for products deemed to have a reasonable probability of causing serious adverse health consequences or death.⁴¹ A study found that of the 465 drugs subject to Class I recall from 2004 to 2012, 237 were identified as dietary supplements.⁴² Although FDA has monitored the marketplace for these potentially unsafe products through facility inspections, underreporting of adverse events and the lack of premarket review mean that products with APIs can enter the market, putting the public's health at risk.⁴³

FDA Action Against Potentially Harmful Supplements

It can take years for FDA to ban the sale of an unsafe dietary supplement. In 1994, it issued the first safety alert on supplements containing ephedra, a dietary ingredient associated with the risk of stroke and possible death.⁴⁴ But the agency did not prohibit sale of supplements that contain this ingredient until 2004.⁴⁵ As a result, consumers were left exposed to unsafe products for 10 years. And despite the ban, FDA continues to identify supplements that contain ephedra, such as Al-Er-G capsules,⁴⁶ which were recalled in May 2017.⁴⁷

Dietary supplements containing 1,3-dimethylamylamine (DMAA) also continue to appear on store shelves, despite safety concerns raised by FDA and the Department of Defense. The department removed dietary supplements with DMAA from military bases in 2011, but it took FDA an additional 16 months to warn consumers about the risks associated with consumption of these products.⁴⁸ Since 2012, FDA has continued to issue warning letters to manufacturers of dietary supplements containing DMAA as the agency has identified them,⁴⁹ notifying them that they are illegally marketing a dietary ingredient that has not been shown to be "reasonably expected to be safe."⁵⁰

Options for enhanced oversight

The current system for regulating dietary supplements has limitations that can put consumers at risk. Consumers and even FDA have little information to help them distinguish between products manufactured under high quality standards and those produced under substandard conditions. To more efficiently monitor the marketplace and take quick action if needed, FDA should have access to more information about the dietary supplement marketplace, such as names of specific products, their ingredients, and product labeling. Supplement manufacturers should have incentives for providing FDA with that information. The agency also needs more resources to carry out enforcement actions. Mechanisms and resources to allow FDA to differentiate between quality supplements and problematic ones would benefit consumers and help protect them from potential harm.

Endnotes

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