



USP Global Public Policy Position

Ensuring the Quality of Dietary Supplements



ISSUE: While dietary supplement use is increasing around the world, there have been quality and safety issues with some products. New approaches are needed to help ensure the integrity of these products, restore confidence, and protect public health.

The use of dietary supplements among consumers is rapidly growing: the global market for these products is projected to reach almost \$180 billion by 2020.¹ In the United States (U.S.), dietary supplements are used by 80% of adults.² Drivers include an aging population, more emphasis on wellness, and a desire by some consumers to economize and exercise control in healthcare choices.

A recently renewed focus on dietary supplement quality and safety has generated discussion around public health implications surrounding these products while also prompting enhanced regulatory interest and enforcement. Concerns have included too little of an active ingredient in a supplement, extraneous material, substitution of a synthetic substance for a claimed naturally derived material, and products adulterated with drugs or drug analogs. There have been reported cases of supplements causing adverse events, including injury to young adults taking products for weight loss or energy.³ Objections have been expressed that dietary supplements can be unsafe or of unknown origin and that the industry needs more oversight.

In the midst of this expanding conversation, there is a growing consensus that new approaches are needed to ensure quality and public trust in dietary supplements and ingredients.

Position: The United States Pharmacopeial Convention (USP)⁴ supports a comprehensive public policy framework to ensure the quality of dietary supplements. The framework should focus on education, investment in the public agencies responsible for consumer protection, public quality standards, and surveillance.

Key elements of a holistic public policy framework to ensure dietary supplement safety and quality include the following:

Empower consumers and healthcare professionals.

1. Increase education campaigns on the importance of dietary supplement quality.

- Public health agencies, enforcement officials, associations, industry, and other organizations should invest in education campaigns that provide guidance on selecting quality dietary supplements and outline potential risks from products whose identity and quality has not been independently assured.
- Consumers should be made aware that independent third-party verification programs can help establish that products and ingredients are what they are represented to be.
- Awareness campaigns should focus on segments of the consumer population that are most vulnerable or likely to experience the most potentially serious physiological effects from poor quality products (e.g., seniors, pregnant women, children, and military/armed forces).⁵

Advance consumer protection.

2. Make adequate public investment in the agencies responsible for ensuring the quality of dietary supplements.

- Protecting consumers by ensuring quality in dietary supplements is a shared responsibility across different agencies at the federal and state/provincial levels.
- Agencies such as FDA and state health departments in the U.S. should be provided with the resources they need to carry out these responsibilities.

Safeguard the consistency and quality of dietary supplements.

3. Ensure that all dietary supplement products adhere to science-based public standards for identity, strength, quality, and purity.

Using public standards to ensure quality⁶ creates certainty for consumers and regulators, advances transparency and fairness within the industry, and also helps keep dietary supplements that are tainted with drugs and drug analogs off the market.

Promote greater transparency for consumers and regulators.

4. Establish “public registries”⁷ that link supplements to public standards and communicate to consumers those that are verified to meet them.

- Registries should utilize a uniform nonproprietary name, linked to a science-based public standard, to provide assurance a product with a certain name is that product and has specified characteristics.

Report quality and safety issues.

5. Enhance surveillance programs, giving policymakers and regulators more information and ensuring more complete tracking of reported adverse events from dietary supplements.

- Enhanced tracking programs can protect consumer safety and help regulators and policymakers determine whether voluntary standards are effective and point to the potential need for an enhanced regulatory framework for quality.

Background

What Are Dietary Supplements?

A dietary supplement is a product taken by mouth and intended to supplement the diet—for example vitamins, minerals, herbs, or other botanicals.⁸ While not always called as such, supplements and other botanical or herbal preparations in various forms have been around for a long time. For example, the Egyptians and Chinese used botanicals over 3,000 years ago for their reputed benefits.⁹ While in some countries dietary supplements are regulated as drugs or as some intermediate category, in other countries, like the U.S., they are regulated as foods.

Why Should We Be Concerned About Supplement Quality?

As the globalization of manufacturing and distribution continues, the need for stronger systems to assess and ensure quality in dietary supplements becomes more pressing. Many dietary supplements and ingredients are made in countries around the world and may be of unknown provenance or may even be mislabeled, problems that can have serious health consequences. For example, Chinese star anise (either as a food ingredient, supplement, or medicinal product) is prized for its reputed health benefits, while Japanese star anise is toxic and can kill a consumer if passed off as the former.¹⁰

In the U.S., clinical and other research studies are not required for dietary supplements; consumers are therefore largely on their own when these products hit store shelves. Adverse reactions, although rare, can be life threatening or even lethal. A lack of understanding of the interactions of dietary supplements with prescription and over-the-counter medicines—as well as with other dietary supplements and foods—may also contribute to products being non-efficacious or even toxic to patients. Healthcare practitioners can be equally disadvantaged in the absence of clinical data and instruction surrounding these products.

According to FDA, the federal agency that oversees the quality of dietary supplements in the U.S., “the choice to use a dietary supplement can be a wise decision that provides health benefits. However, under certain circumstances, these products may be unnecessary for good health or they may even create unexpected risks.”¹¹ FDA notes that people choosing to supplement their diet with herbals, vitamins, minerals, or other substances may want to know more about the products they choose so they can make informed decisions. The agency provides helpful tips for dietary supplement users, including for seniors.¹²

In the U.S. in early 2015, concerns about the quality and safety of dietary supplements resulted in an investigation by the New York State Attorney General’s Office into herbal supplement manufacturers and sellers. The investigation spread to several other states and generated calls by industry and some lawmakers for greater application of existing federal law—and ultimately saw a multiagency federal enforcement action. The enhanced regulatory attention also prompted efforts by industry to show greater responsiveness and accountability, including advancing proposals for heightened public information (“registries”)¹³ about dietary supplements and ingredients. Incidents also generated retailer interest in learning how to ensure the quality of supplement products on their shelves.

Outside the U.S., a number of countries, including India and China, have been separately seeking to update and expand regulation of dietary supplements.

How Are Dietary Supplements Regulated for Quality?

Global Situation

Around the world, dietary supplements may be regulated as foods or drugs, or sometimes a hybrid. For example, CoQ10, considered a dietary supplement in the U.S., is included in the Japanese Pharmacopoeia and regulated as a drug; similarly, the European Pharmacopoeia has monographs for Echinacea as a drug, while it is treated as a supplement in the U.S. At the same time, many countries have an intermediate category of “traditional medicines” with different requirements for registration than those required for drugs.

Some countries have recently determined that there is a need to create a new regulatory framework for dietary supplements (and such similar products). In some cases, international agencies are creating regulations similar to those found in the U.S., but generally they are more stringent.

Examples of international regulatory requirements for dietary supplements that are not mandatory in the U.S. include

- Registration,
- Premarketing approval of chemical and manufacturing controls, and
- Premarketing review of safety and benefit claims.

Examples of recent international proposals include India’s draft regulation on “Food or Health Supplements, Nutraceuticals, Foods for Special Dietary Uses, Foods for Special Medical Purpose, Functional Foods, and Novel Foods,”¹⁴ which seeks to improve labeling requirements for food and supplements and references various nations’ compendia and other sources, and China’s final revision of its 2009 Food Safety Law specifying registration and notification requirements governing special foods such as health foods (i.e., dietary supplements).¹⁵

The United States

In the U.S., the Dietary Supplement Health and Education Act (DSHEA; Public Law 103-417, October 25, 1994) provides a regulatory framework for manufacturing and marketing dietary supplements that are intended to supplement the diet and contain dietary ingredients (vitamin, mineral, herb or other

botanical, amino acid, or a concentrate, metabolite, constituent, extract, or combination of any of these ingredients).

Under DSHEA, dietary supplement manufacturers are responsible to establish the safety and quality of a product, but are not required to share that information with FDA before the product enters the market unless it contains a new dietary ingredient, defined as a dietary ingredient that was not marketed in the U.S. in a dietary supplement before October 15, 1994.¹⁶ To date, FDA has not issued final guidance on what constitutes new dietary ingredients, although it has issued final guidance on distinguishing liquid dietary supplements from beverages.¹⁷

Special Challenges for FDA

While FDA has the authority under DSHEA to remove a product from the marketplace if it presents “significant or unreasonable risk of illness or injury,” FDA is first charged with the responsibility to prove that the product presents such a risk to public health. Because FDA has limited resources in ascertaining harm, and many of these products also have an inherently high threshold for safety, products of unknown quality and unestablished safety can *de facto* be marketed in the U.S. without any oversight.

The U.S. Government Accountability Office (GAO)¹⁸ has called on FDA to do a better job in tracking serious adverse events related to dietary supplements, including utilizing data from poison centers, in addition to its present sources (industry reports). At least one Congressional committee has called for clarification of whether retailers feel they are obligated under DSHEA to report adverse incidents, noting this as a possible weak link in the adverse reporting chain.¹⁹

FDA is able to catch noncompliant facilities on inspection—in fact, more than 50% of inspections lead to agency observations/warning letters. But finding offending products can be a resource-intensive activity. The agency needs more resources to ascertain compliance and undertake enforcement.

Although identity testing is required by FDA regulations,²⁰ manufacturers can develop and/or choose the standards to which they test. Because there are few uniform requirements²¹ and no FDA premarketing oversight, many of these testing standards remain private and unknown to the public. This makes it difficult for a consumer or other concerned party to compare the “same” product (e.g., Echinacea) made by two different manufacturers. In fact, the quality of dietary supplements may vary significantly from one manufacturer to another, or even within a single brand—without uniform standards it is hard to know for sure.

Opportunities for Manufacturers and Regulators

- USP’s compendial quality standards are published in the *United States Pharmacopeia–National Formulary (USP–NF)*, an official compendium of the U.S.
 - *USP–NF*’s drug quality standards are legally enforceable by FDA for over-the-counter and prescription drugs under the adulteration and misbranding provisions of the Federal Food, Drug, and Cosmetic Act.
 - *USP–NF*’s dietary supplement and dietary ingredient standards are legally enforceable by FDA for products that are voluntarily labeled as meeting “USP.” In that respect, *USP–NF* is also an official compendium for dietary supplements in the U.S., although it is not recognized for dietary supplements in the same way as for drugs.
- Following USP compendial quality standards for dietary supplements can help manufacturers establish adherence to Good Manufacturing Practices (GMPs) and provide assurance that ingredients they use are of good quality.
- Testing to science-based public quality standards can help ensure that manufacturers and regulators are comparing products to a standard of quality.
- Voluntary verification programs²² based on public standards can help ensure that what’s on the label is in the bottle in the right purity and strength.

APPENDIX I: Regulation of Dietary Supplements Outside the U.S.²³

Argentina requires registration of dietary supplements prior to marketing; therapeutic claims not scientifically supported are not allowed.²⁴

Australia uses the category of “complementary medicines,” essentially classified as drugs, with categories based on health risk. Manufacturers are required to hold a manufacturing license.²⁵

Brazil uses the category of “vitamin or mineral supplement.” Registration is required, subject to the same registration requirements as food. Claims to prevent, alleviate, or treat a disease are prohibited.²⁶

Canada uses the category “natural health products,” classified like drugs as Therapeutic Products. Registration is required, but premarketing is allowed prior to approval. Health claims are acceptable provided the product is registered.²⁷

China uses the category “health food,” classified as food, dietary supplement, or Traditional Chinese Medicine (TCM) on a case-by-case basis. All health food products sold within China must be approved and registered with the China Food and Drug Administration (CFDA), which will assess and examine the security, effectiveness, and quality control and labeling of products. A health food can promote only its approved health function(s) on its label and advertisement (e.g., enhancing immune functions, assisting blood lipids reduction, assisting blood sugar reduction, assisting memory improvement).²⁸

The European Union uses the category “food supplements,” classified as foods. Food supplements are concentrated sources of nutrients or other substances with a nutritional or physiological effect whose purpose is to supplement the normal diet. They are marketed “in dose” form (i.e., as pills, capsules, liquids in measured doses per ESFA definition). Registration is not required, but for harmonization purposes, there is a list of permitted vitamin or mineral preparations that may be added for specific nutritional purposes in food supplements; the marketing of products containing vitamins and minerals not listed is prohibited. Functional claims are allowed.²⁹

India uses the category “foods for special dietary uses,” with the subcategories “functional food,” “nutraceutical supplement,” or “health supplement.” The product cannot claim to mitigate or cure any specific disease but certain health benefit claims are permitted.³⁰

Japan uses the categories “foods for specific health use” (FOSHU) or “food and nutrient functional claims” (FNFC) based on their product claims. No government approval is required for FNFC claims, because they are standardized and preapproved. FOSHU claims must provide evidence to the government of the product’s physiological effect, quality control processes, and safety prior to marketing. Standardized and approved claims are permitted for FNFC products. FOSHU claims are permitted after government approval.³¹

Jordan uses the categories “herbal medicines,” “herbal food products,” “vitamin and mineral products,” “food supplement,” or “herbal medicine product,” and the product is considered a drug or food depending on how it is classified. Herbal medicines, herbal products, and vitamins and minerals products require registration. Medical, health, nutrient content, and structure/function claims are allowed.³²

Mexico uses the category “nutritional supplements,” and they are classified as foods. Registration is not required. Claims are not permitted to be used on food supplement products. Its only intended use is to increase total dietary intake; complement it or replace any component; or treat a disease, symptom, or condition.³³

New Zealand uses the categories “natural health products,” “complementary medicines,” and “dietary supplements.” New Zealand is currently working jointly with Australia to implement a scheme to regulate “complementary medicines,” with the intent to create a national registry for these products.³⁴

Nigeria uses the category “herbal medicines,” classified as dietary supplements, health foods, functional foods, or as an independent regulatory category. Herbal medicines are required to be registered and are sold without restriction by licensed practitioners. Claims that may be made about herbal medicines include health, nutrient content, and structure/function claims.³⁵

Russia uses the category “biologically active food supplements” (BAFS). Food is divided into nutraceuticals and parapharmaceuticals but cannot contain psychotropic or narcotic substances. Advertisement of BAFS is strictly controlled, and no claims to treat or cure diseases are allowed.³⁶

South Africa uses the categories “traditional and complementary medicines,” classified as foods or drugs. Registration is required. Claims are allowed and classified into two categories: 1) high: treat cure/manages disease disorder; or 2) low: health maintenance and enhancement, including nutritional support not related to specific disease claim.³⁷

Turkey uses the category “herbal pharmaceutical product” but is in the process of harmonizing with an European Commission Directive and renaming these substances as food supplements. They are classified as Non-prescription medicinal, and include phytopharmaceuticals, nutraceuticals, cosmeceuticals, and herbal teas. Registration is required. Recommended use claims are allowed but inclusion of statements like “prevents or cures disease” on labels is prohibited.³⁸

APPENDIX II: How USP Works With Industry to Promote the Use of Quality Standards and Help Safeguard Dietary Supplements

USP offers tools to help manufacturers and suppliers safeguard the dietary supplement supply in the global marketplace and determine the identity and quality of supplements and ingredients.

USP Standards

To assist industry in the development and testing of dietary supplements, USP offers documentary standards (written monographs that describe specifications and tests for identity, strength, quality, and purity) and Reference Standards³⁹ (highly characterized substances intended for use in conducting the quality control tests and analytical procedures associated with documentary standards).

USP standards help limit the introduction of potential adulterants and contaminants and serve as a widely acknowledged quality benchmark in the buying and selling of dietary supplement products and their ingredients.

The *United States Pharmacopeia–National Formulary (USP–NF)* is an official compendium of the United States for drugs and dietary supplements. USP’s compendial quality standards are set through leading scientific expert volunteers, with participation of U.S. government liaisons from FDA.

The USP Catalog features more than 3,600 items, including more than 800 dietary-supplement-related monographs and approximately 200 Reference Standards for dietary supplements (e.g., amino acids, botanicals, vitamins and minerals, and fish oils).

Independent Verification Services

In addition to its standards-setting work, USP offers the industry voluntary, independent, third-party verification services for dietary supplement finished products and dietary ingredients.⁴⁰



The **USP Verified Mark** is a symbol awarded by USP to dietary supplement products that meet the stringent criteria of its Dietary Supplement Verification program (aligned to USP compendial standards). The Mark has appeared on more than 400 million supplement labels since the program’s start in 2002—helping ensure that what’s on the label is in the bottle in the right purity and strength.



USP also has a new **GMP Facility Audit Program** for dietary supplement and dietary ingredient manufacturers.⁴¹ The program helps ensure that manufacturers have good quality systems and may also help mitigate regulatory risks by preparing manufacturers for GMP inspection.

Meetings, Courses, Workshops, and Roundtables

USP meetings, courses,⁴² workshops, and roundtables bring together the world’s leading scientific, regulatory, and healthcare experts to share knowledge, lead discussions, and provide insight for the effective development and application of standards. USP offers various dietary-supplement-related educational programs for industry, practitioners, and others,⁴³ including online and classroom training.⁴⁴ USP’s offerings have featured a course on food fraud mitigation, including USP guidance in this area; a workshop on adulteration, making available the expertise of authorities drawn from government and other sources;⁴⁵ and an Expert Panel roundtable meeting on adulteration.⁴⁶

Stakeholder Forums and User Forums

USP hosts Dietary Supplement Stakeholder Forums and User Forums—offering manufacturers, organizations, service providers, and other interested parties who work with dietary supplements the opportunity to share perspectives, provide direct feedback on priority standards issues,⁴⁷ and learn about USP initiatives and how to use USP resources.⁴⁸

E-Newsletters

USP sends out via email periodic news about dietary supplement standards, as well as industry hot topics with links to upcoming meetings and events.⁴⁹ Individuals are welcome to sign up for this free service.

Food Fraud Database

USP offers a Food Fraud Database as a resource to industry, government, academia, and consumers.⁵⁰ Beyond listing food fraud adulterants, the database provides a baseline understanding of the susceptibility or vulnerability of individual ingredients to fraud. In addition, it can be useful for those managing the risk of food fraud by providing a library of detection methods reported in peer-reviewed scientific journals. Because an ingredient can variously be a food ingredient, dietary ingredient, or excipient, the database can be a helpful resource to those interested in maintaining the quality of dietary supplements or ingredients.

¹ <http://globenewswire.com/news-release/2015/04/23/727513/10130416/en/Dietary-Supplements-Market-is-Expected-to-Reach-US-179-8-Billion-Globally-in-2020-Persistence-Market-Research.html>

² <http://oig.hhs.gov/oei/reports/oei-01-11-00211.pdf>

³ A study in the *New England Journal of Medicine* reported more than 20,000 emergency room visits a year from injuries caused by dietary supplements, <http://www.nejm.org/doi/full/10.1056/NEJMsa1504267>

⁴ USP is a nongovernment, nonprofit organization that was founded in 1820 with a mission to improve global health through public standards and related programs. USP standards are set through leading scientific expert volunteers, with participation of government liaisons from the U.S. Food and Drug Administration (FDA).

⁵ Rand Center for Military Health Policy Research, Regulation of Dietary Supplements in the Military, Report of an Expert Panel, http://www.rand.org/content/dam/rand/pubs/conf_proceedings/2011/RAND_CF288.pdf

⁶ U.S. FDA regulations permit supplement manufacturers to choose the standards to which to test. These standards can remain private and unknown (see footnote 21). USP recommends that dietary supplement manufacturers and regulators adhere to science-based public standards.

⁷ The concept of “registries” has been advanced by industry, <http://www.naturalproductsinsider.com/blogs/supplement-perspectives/2015/11/voluntary-registry-for-dietary-supplements-next-s.aspx>. While such concepts are still being fleshed out, as described, they would involve a publicly available catalogue of information (database) about dietary supplements and ingredients, with such information likely being offered voluntarily by industry and maintained by a yet-to-be-determined party or parties. To be useful and effective, registries must have the characteristics described in recommendation 4, and be comprehensive and publicly accessible, whether operated by the private sector, government, or some other entity.

⁸ <http://www.fda.gov/AboutFDA/Transparency/Basics/ucm195635.htm>

⁹ <http://umm.edu/health/medical/altmed/treatment/herbal-medicine>

¹⁰ <http://www.ahpa.org/Default.aspx?tabid=326>

¹¹ <http://www.fda.gov/Food/DietarySupplements/UsingDietarySupplements/ucm110567.htm>

¹² <http://www.fda.gov/Food/DietarySupplements/UsingDietarySupplements/ucm110493.htm>

¹³ See footnote 7.

¹⁴ http://fssai.gov.in/Portals/o/Pdf/Draft_Regulation_on_Nutraceuticals_WTO_23_07_2015.pdf

¹⁵ https://www.cov.com/~media/files/corporate/publications/2015/05/china_issues_revised_food_safety_law.ashx

¹⁶ Federal Food, Drug, and Cosmetic Act, 413(d).

¹⁷ Guidance for Industry: Distinguishing Liquid Dietary Supplements from Beverages, <http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/DietarySupplements/ucm381189.htm>

¹⁸ GAO, DIETARY SUPPLEMENTS, FDA May Have Opportunities to Expand Its Use of Reported Health Problems to Oversee Products, GAO 13-244, March 18, 2013.

¹⁹ Letter from Ranking Member Claire McCaskill, Senate Special Committee on Aging to retailers, June 2015.

²⁰ 21 CFR 111.70, 111.75.

²¹ FDA’s Dietary Supplement GMPs: Standards Without Standardization, 63 *Food and Drug Law Journal*, 929–942, 2008.

²² See, e.g., <http://www.usp.org/usp-verification-services>

²³ Condensed from USP internal research, current as of October 17, 2014.

²⁴ ANMAT, http://www.anmat.gov.ar/principal_en.asp

²⁵ TGA, <http://www.tga.gov.au/overview-regulation-complementary-medicines-australia>

²⁶ ANVISA

²⁷ Health Canada, <http://laws-lois.justice.gc.ca/eng/regulations/SOR-2003-196/>

²⁸ CFDA, <http://eng.sfda.gov.cn/WS03/CL0755/>

²⁹ EFSA, http://ec.europa.eu/food/safety/labelling_nutrition/supplements/index_en.htm

³⁰ www.fssai.gov.in/GazettedNotifications.aspx#regulations2011

³¹ <http://www.mhlw.go.jp/english/topics/foodsafety/fhc/02.html>; <http://www.mhlw.go.jp/english/topics/foodsafety/fhc/01.html>

³² JFDA

³³ <http://www.cofeprib.gob.mx/Paginas/Idiomas/Ingles.aspx>; <http://www.cofeprib.gob.mx/Paginas/Suplementos%20Alimenticios/%C2%BFQue-son-los-suplementos-alimenticios.aspx> (Spanish)

³⁴ ANZTPA

³⁵ NAFDAC

³⁶ Roszdravnadzor, Rospotrebnadzor

³⁷ MCCZA

³⁸ IEGM

³⁹ <http://www.usp.org/dietary-supplements/reference-standards>

⁴⁰ <http://www.usp.org/usp-verification-services>

⁴¹ <http://www.usp.org/news/dietary-ingredient-and-supplement-manufacturers-can-demonstrate-superior-quality-systems-using-newly-launched-united-states>; <http://www.usp.org/dietary-supplements/verification-services/gmp-facility-audit-program>

⁴² <http://www.usp.org/meetings-courses>

⁴³ <http://www.usp.org/usp-verification-services/usp-verified-dietary-supplements/healthcare-professionals> (see section titled “Dietary Supplement Quality Education Programs”)

⁴⁴ http://www.usp.org/sites/default/files/usp_pdf/EN/meetings/usp-education-course-catalog.pdf (see page 12 of the catalog)

⁴⁵ <http://www.usp.org/meetings-courses/workshops/adulteration-and-fraud-food-ingredients-and-dietary-supplements-attend-two-key-learning-events>; see also https://uspharmacopeia.csod.com/LMS/catalog/Welcome.aspx?tab_page_id=-67&tab_id=20000339

⁴⁶ See e.g., <http://www.usp.org/meetings-courses/expert-committee-meetings/adulteration-expert-panel-roundtable-meeting>

⁴⁷ <http://www.usp.org/meetings-courses/stakeholder-forums/dietary-supplements-ds/meeting-2-2014>

⁴⁸ <http://www.usp.org/meetings-courses/user-forums>

⁴⁹ <http://www.usp.org/store/free-resources/newsletter-and-information>

⁵⁰ <http://www.foodfraud.org/>