Food supplements marketed worldwide: a comparative analysis between the European and the U.S. regulatory frameworks

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Abstract: In recent decades, a new health paradigm emerged which increasingly places diet and nutrition at the center of citizens' healthcare. The resulting evolution of the food market has prompted country governments to adapt their regulatory frameworks to ensure product safety and preserve the health of citizens. Dietary supplements (DS) are products which are increasingly occupying a significant market share in Western countries, contributing to meeting the nutritional and physiological needs of a large portion of the global population. Food supplements must be safe for use by the final consumer who has access to the global market, but currently they are framed by a different legislation worldwide. This search aimed of comparing the legislative frameworks currently in force in the European Union (EU) and in the United States (USA), the two main markets in which DS are purchased, to focus on the strengths, similarities and possible shortcomings, against the backdrop of a global market which often transcends the regulatory barriers of individual countries. Both in the EU and the USA, food supplements are governed by specific regulations to ensure their safety and quality. However, the regulatory approaches differ sharply in some cases. It is expected that more and more operators will launch new DS in Western markets. As a result, it is crucial for competent authorities in food safety to deepen and develop additional regulatory tools aimed to control and safeguard the DS market.

Highlights

- The resulting evolution of the food market has prompted country governments to adapt their regulatory frameworks to ensure food safety and safeguard the health of citizens
- Food supplements must be safe for use by the final consumer who has access to the global market, but currently they are framed by a different legislation worldwide
- Both in the EU and the USA, the two main markets in which DS are purchased, food supplements are governed by specific regulations to ensure their safety
- Nevertheless, the regulatory approaches differ sharply in some cases
- As a result, it is crucial for competent authorities to develop additional regulatory tools aimed to control and safeguard the DS market

Key words: dietary management, food supplements, regulatory framework, comparative legislation

Introduction

Having an equilibrate diet has become central in preserving citizens' health in most of western countries [1]. Consequently, the food industry evolved from suppliers of essential goods for human nutrition to providers of food-derived products, enriched with novel substances with health effects able to provide a nutritional supplementation of people body's functions. In parallel, the globalization has enlarged the international foods' movements, permitting to exotic foods to reach markets and consumers never reached before. Such an evolution of the food market has pushed authorities to adapt their regulatory framework to ensure the safety

of products and to preserve citizens' safety. On one side, the increased availability of exotic foods forced the regulatory authorities to lighting up borderline situations, avoiding the marketing of products containing molecules with a pharmacological action. On the other side, the increased interest of the healthcare community for nutritional aspects in the treatment and prevention of human diseases and the regulatory qualification of foods have increased its complexity over the years in order to distinguish among foods, foods for specific groups of populations, foods enriched of substance not naturally present in them, products intended to integrate the standard diet like food supplements (FS)/dietary supplements (DS) [2,3]. They must be safe for use by the final consumer, and currently they are framed by a different legislation in the United States of America (USA), in the European Union (EU), in the Asia Pacific countries or in other realities worldwide [4]. Among foods, DS belong to the category of products most marketed worldwide and most purchased by consumers [5-7]. However, people often refer to DS without having clear the regulatory framework to which they belong regarding food safety field [8]. In addition, to date there is no globally harmonized definition regarding the category of products known as nutraceuticals, natural products, products that often, from a regulatory perspective, are actually DS [9]. Furthermore, it is noteworthy that a product which is considered a food supplement and regulated as food under a specific regulation may be considered a medicinal product if placed under another legislative framework [7-10]. From the above, the present review is aimed at comparing the present legislation between USA and EU, the main DS markets, to focus on the strengths, similarities and possible shortcomings, against the backdrop of a global market, which often transcends the regulatory barriers of individual countries.

Food supplements global market

The global DS market is a rapidly growing industry, with a market size of approximately $140 billion in 2020 [5]. The market is driven by an increasing focus on preventive healthcare by aging populations and growing interest by people in fitness and wellness. In fact, the global DS market has been on the rise in recent years due to increasing health concerns and rising awareness among consumers about the benefits of supplements [1,5,6,8]. Vitamins and minerals are the largest product categories, accounting for around 35% of sales, followed by botanicals and herbal supplements. North America is the largest regional market, followed by Europe and the Asia Pacific [11,12]. In parallel, online sales are increasing in popularity, due to several factors, such as the convenience and the COVID-19 outbreak [5,13-15]. In the USA, the DS market has been steadily growing, with a current estimated value of over $30 billion. Vitamins and minerals are the most commonly consumed DS also in the USA. However, other categories, such as herbal supplements and sports nutrition products, have also seen significant growth in recent years. Online sales of DS have also been on the rise in the USA, with consumers preferring the convenience of online shopping and the availability of a wider range of products. In the EU, the FS market has also been growing, with a current estimated value of over €12 billion [11]. The demand for FS in the EU is driven by similar factors as in the USA, such as increasing health concerns and interest in preventive healthcare: vitamins and minerals are also the most commonly consumed FS in the EU. Overall, a number of factors caused an increase in the FS/DS consumption in Western populations in recent years, but in particular the COVID-19 outbreak has largely stimulated the sale and purchase of FS/DS in the USA and the EU, regions where the dietary supplement industry is largely concentrated [13]. Therefore, the market is expected to see a further increase in the demand for immunity-boosting supplements, and the global dietary supplements market size is expected to expand at a compound annual growth rate of about 8.9 % until 2030 [11].

Legislative frameworks

Class of food derivates

As well as for other foods, such as foods for special medical purposes or gluten-free foods, the regulatory framework applicable to FS in Europe is particularly stratified. As other foods, the regulatory framework on FS is constituted both by acts applicable to all foods and those more specific for such regulatory class. In particular, since FS are essentially foods for the EU legislation, the Regulation (EC) no. 178/2002 is applicable to them. Such Regulation establishes the principles and general requirements of the food law laying down European competences and procedures in the field of food safety, with the aim at guaranteeing a high level of protection either for human health or for the interest of consumers in relation to food [16]. In light of the

regulation, food is defined as "any substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be ingested by humans". The term "food" includes beverages, chewing gum and any substance, including water, intentionally incorporated into food during its manufacture, preparation or processing. The term "food" does not include feed, live animals unless they are prepared for placing on the market for human consumption, plants before harvesting, medicines under Council Directives 65/65/EEC and 92/73/EEC, tobacco and tobacco products under Council Directive 89/622/EEC, cosmetics products, residues, and contaminants. The FS are regulated also by Directive 2002/46/EC, which defined them as foods intended to supplement the normal diet and which constitute a concentrated source of nutrients or other substances having a nutritional or physiological function (art. 2). FS can be developed both mono- and multi-compounds, in pre-measured forms, e.g., capsules, tablets, liquids contained in vials, dropper bottles and other similar forms of liquids and powders intended to be taken in small unit quantities [17].
In the USA, dietary supplements are regulated by most of same provisions of law that are applied to foods, the Federal Food, Drug and Cosmetic Act 4. However, following amendments passed by Congress in 1994, known as the Dietary Supplement Health and Education Act (DSHEA), DS are also subjected to specific provisions that do not apply to conventional food [18,19]. DSHEA defined DS any products intended to supplement the diet. Moreover, DSHEA determined that DS can take the form of conventional food-like cereal, candy bars - but cannot represent themselves as a conventional food. The definition of DS is contained in the section 201 of the Federal food, drug, and cosmetic act (FD & C Act) [19]. In particular, the definition quotes that "a dietary supplement….is a dietary substance for use by man to supplement the diet by increasing the total dietary intake". This definition restricts the scope of substances to be included in DS and called "dietary ingredients", potentially including all food additive substances but excluding substances previously approved as active ingredients with pharmacological activity [19-20].

Content of ingredients and substances characterizing the composition of food and dietary supplements

The ingredients characterizing the composition of FS may be vitamins, minerals, plants or other substances like amino acids, fibers, probiotics, prebiotics. Overall, in the EU 'other substances' are defined in article 2 of Regulation (EC) 1925/2006 as "substances other than vitamins and minerals with a nutritional or physiological effect", whereas vitamins and minerals and their forms that may be added to foods, including FS, are listed in Regulation (EC) 1170/2009, amending Directive 2002/46/EC [21-22]. According to the regulation, the minimum level of vitamins and minerals present in FS must be significant, thus at least 15% of the nutritional reference value (NRV); maximum levels are not currently harmonized in the EU. However, the expected daily intake limits for vitamins, minerals and the other ingredients contained in FS may be regulated at the level of individual countries, based on scientific risk assessments. For instance, in Italy, reference is made to some lists drawn up by Competent Authority (CA) which includes the threshold of the daily intake foreseen for vitamins and minerals in FS, and other substances other than vitamins and minerals having a nutritional or physiological effect, allowed to be used in FS [23]. Similarly, a list of plants and related plant parts that can be used in foods and thus in FS has been released in Belgium, France and Italy, depending on particular properties, which the plants have to maintain specific nutritional or physiological activities. Where established, limits of allowable intake with daily dose and additional warnings are also given, based on risk assessments carried out. This was an international initiative which involves several EU member states and was drawn up by Belgium, France and Italy as the first step in an agreed project to achieve a common framework on the use of plants and derivatives in the field of food supplements, with the aim of also promoting harmonization of the subject at the European level [24]. Further specific provisions for the regulation of 'other substances' are outlined in article 8 of Regulation (EC) 1925/2006 which provides a procedure to address the safety concerns associated with any sub-stances other than vitamins and minerals used in food, including FS [21]. In particular, the EU Commission may initiate the 'Article 8 procedure' in order to include a certain substance on a list to prohibit (Annex III Part A), restrict (Annex III Part B) or to put it under community scrutiny to be reviewed within 4 years (Annex III Part C). Among the ingredients in the FS, all the food products or substances, vegetables preparations or extracts without significant consumption history before May 15, 1997 qualify as novel foods under Regulation (EU) 2015/2283 [25]. All the novel foods need to be authorized by the European Commission (EC), after the assessment of safety carried out by the European Food Safety Authority (EFSA). Furthermore, the Commission Implementing Regulation (EU) 2017/2470 (Union List of authorized novel foods) establishes a list of all the authorized novel foods in the EU, including their conditions of use, labelling requirements and their specifications, and it is amended following each new authorization.

In the USA, unlike other categories of products, which are classified according to their intended use, such as medicines or cosmetics, in order to be regulated as a DS a product must contain at least one of the following dietary ingredient listed in the FD & C Act: vitamin, mineral, botanical, amino acids, acids or other dietetic substances used by humans to supplement the diet by increasing total dietary intake or concentrates, metabolites, constituents, extracts or combinations of these ingredients. Therefore, if a product does not contain any of the above ingredients, it does not meet the definition of a DS [19,26]. Current U.S. regulations do not prohibit the marketing of dietary supplements containing pharmacologically active molecules. However, any substance approved as a new drug is excluded from the definition of a dietary supplement, unless the item was marketed as a dietary supplement or food prior to its approval as a new drug [27-28]. Moreover, the Food Business Operator (FBO) must notify the Food and Drug Administration (FDA) before marketing products with new dietary ingredients (NDI). Manufacturers of NDI must notify FDA 75 days prior to the introduction of a DS containing the ingredient into the market. NDI are defined as ingredients that have been not marketed in the USA prior to October 15, 1994 [19,26]. Any required notification must include information on which FBO have based their conclusion of a reasonable expectation of safety. Furthermore, based on the DSHEA safety standards, the FDA maintains the authority to recall certain ingredients from the market, for example in the case of products containing the Chinese herb ma huang (Ephedra sinensis) in 2004, based on the determination of "risk unreasonable" for health [29].

Place on the market

Both in the EU and the USA, FS and DS do not require a formal authorization by a competent authority, as for medicinal products, for being placed on the market.
In the EU, FS are subject to a notification procedure, where the manufacturer notifies the competent national authority of their intention to market the product. Only in the case of FS containing novel or innovative ingredients, falling under the Novel Foods Regulation or if its label contains a health claim falling under the Regulation 1924/2006, pre-market authorization should be obtained.
DS in the United States are regulated by the FDA, but do not require FDA pre-market approval or a pre-market notification process.

Manufacturing

The FS production in the EU and USA markets involves a series of regulatory processes to ensure their safety and quality. In Europe, under Regulation (EC) n. 178/2002 and Directive 2002/46/EC, the production and packaging of FS follow the provisions generally established for foods. As an example, they are subject to the approval of the manufacturing and/or packaging establishment with the competent national health authority: e.g., in Italy such aspects are regulated at local level. The FBO that notifies and places the product on the market is obliged to include on the label the mandatory indication of the FBO responsible for ensuring product's compliance with the regulations, complete with name and address. In cases where production is outsourced to a third party, priority should be given to information on the responsible FBO. Any secondary information may follow that relating to the responsible FBO. As stipulated in the regulations, all operators who are involved in the food production chain of post-primary sectors must apply self-control to production in a rational and organized manner, according to the principles of HACCP (Hazard analysis and critical control points). The HACCP system is a tool intended to help FBOs achieve a higher level of food safety. The plan should aim to prevent the causes of nonconformities before they occur and should provide for appropriate corrective actions to minimize risks when, despite the implementation of preventive measures, nonconformity occurs. The main objective is to establish a documented system by which the FBO can demonstrate that it has operated in a way that minimizes risk under its own responsibility.
In the USA, DS manufacturing facilities are subject to the same registration requirements applicable to food manufacturing facilities per the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 additions to section 410 of the Federal Food, Drug, and Cosmetic act. Moreover, regulatory requirements for ingredient quality in DS are codified in 21 CFR Part 111 (Current Good Manufacturing Practice in Manufacturing, Packaging, Labelling, or Holding Operations for Dietary Supplements) [30]. These regulations define "quality" to mean that the DS consistently meets the specifications established for identity, purity, strength, and composition, and adheres to limits on contaminants [31]. Manufacturers are required to follow Good Manufacturing Practice (GMP) guidelines for the production, packaging, labeling, and storage of DS. Compliance with FDA GMP regulations is essential to ensure product safety and quality. The GMP

regulations, aimed at achieving comprehensive quality systems, require manufacturers to verify that laboratory examination and testing methods are appropriate for their intended use and to scientifically identify and use validated and appropriate methods for each established specification [32].

Labelling and claims

By understanding the regulatory framework behind claims and label statements, consumers can make more informed decisions and health care professionals can better assist their patients.
Overall, in the EU European Regulation 1169/2011 broadly defines the principles, requirements and responsibilities governing mandatory food information and, in particular, food labeling. Furthermore, as required by article 6 of Directive 2002/46/EC, FS labeling bears the following mandatory elements: the name of the nutrients that characterize the product, the recommended daily intake, a warning not to exceed the recommended dosage, a statement that supplements are not intended as a substitute for a varied diet, eventually that they should be kept out of the reach of children under three years of age. Furthermore, the same article requires that the food information cannot attribute to these products the property of preventing, treating or curing a human disease or relate to such properties. Claims allowed to the FS labels are classified in health and nutritional claims. Overall, Regulation 1924/2006 establishes the rules for the use of nutritional and health claims, which can be claimed voluntarily by FBO on foods labels, and thus in particular on FS [33]. The purpose of the regulation is to harmonize the legislation of the Member States, to promote innovation, to favor the free circulation of foods and fair competition between operators as well as to guarantee clear, truthful and science-based information, with the aim at guiding and protecting the consumer, encouraging conscious choices. When referenced to nutritional indications, it means any indication which states, suggests or implies that a food owns particular beneficial nutritional properties, due to the energy it provides and the nutrients it contains or does not contain. On the other hand, when referenced to health claims, it means any claim which states, suggests or implies the existence of a relationship between a specific food component and health. Health claims are classified in health claims other than those on the reduction of risk of disease, health claims relating to decreasing the risk of disease and health claims relating to the health and development of children. Both health and nutritional claims which can be used in the FS labeling must be authorized in advance by EC supported by EFSA, that, on the basis of the scientific evidence, which may support the use of a particular claim, provides a positive or negative opinion on its use. For the purpose of proper communication to the consumer, without prior authorization, no claim can be used by the FBO. The list of claims authorized by the EC with their regulatory references is public and available for consultation by all European citizens [34].
In the USA, the FBO is responsible for the safety and labeling of the marketed product. As required by the Act, manufacturers cannot make specific claims about disease treatment, only with reference to nutritional support and any information related to physiological functions. Regulations cover three types of claims for food and dietary supplements: health, nutrient content and structure/function claims [18,35-37].
Health claims describe the relationship between a food substance and reduced risk of a disease or health-related condition. The FDA oversees health claims on food and dietary supplement labels through three main avenues: the 1990 Nutrition Labeling and Education Act (NLEA), the 1997 Food and Drug Administration Modernization Act (FDAMA), and the FDA's Interim Procedures for Qualified Health Claims.

- NLEA Authorized Health Claims are based on scientific evidence reviewed by the FDA. They must meet a significant scientific agreement standard, for instance how the intake of a mineral may reduce the risk of a specific illness
- Health Claims Based on Authoritative Statements (FDAMA) can be authorized based on authoritative statements from recognized scientific bodies or government agencies. These claims are not applicable to dietary supplements. Firms must submit notifications to the FDA, and these claims can be used after 120 days unless the FDA objects.
- When scientific evidence is emerging but not conclusive, the FDA reviews petitions for qualified health claims. If the evidence is credible, the FDA issues letters of enforcement discretion with qualifying language to prevent misleading consumers. These claims indicate that supporting evidence is limited.

A health claim must include two components: a substance (food, food component, or dietary ingredient) and a disease or health-related condition. Statements lacking these components are considered dietary guidance or structure/function claims and do not require premarket review by the FDA.

Structure/Function Claims describe the role of a nutrient or dietary ingredient in maintaining normal body structures or functions. Unlike health claims, these do not link the nutrient to disease prevention and do not require FDA pre-approval. Manufacturers must substantiate these claims and notify the FDA within 30 days of marketing. Structure/function claims for conventional foods focus on nutritive value effects, while those for dietary supplements may include non-nutritive effects. Dietary supplements with structure/function claims must include a disclaimer that the FDA has not evaluated the claim and that the product is not intended to diagnose, treat, cure, or prevent any disease.
Nutrient Content Claims are authorized by the NLEA, and describe the level of a nutrient in a product using terms like "free," "high," "low," or comparative terms like "more," "reduced," "lite." Such claims must comply with FDA regulations to ensure consistency and meaning for consumers, for instance how a specific quantity of a mineral may imply a low level and must meet criteria for such a claim.

Distribution and consumers' access to products

In the EU, FS are widely available and can be purchased from various outlets, including pharmacies, supermarkets, and online platforms. The purchase of FS can be made without the need to have a doctor's prescription. On the other hand, there are several diseases such rare diseases but also more common diseases, as hypertension, that need a specific dietary management of the illness [38,39]. Thus, in some cases people suffering from pathologies or medical conditions that determine a nutritional vulnerability need the taking of FS, in conjunction with administration of medicine. Therefore, in these cases in some European countries, FS can leverage the reimbursement through the national health services, which ensure the continuity of care to patients who need an integrative care.
In the USA, DS are widely available and can be bought at different points of sale, including pharmacies, supermarkets and online platforms. DS may be purchased without the need for a physician's prescription. DS cannot be reimbursed through American Flexible Spending Accounts. However, in patients with a specific medical condition diagnosed by a physician, DS recommended by a doctor as treatment for this condition are tax-deductible medical expenses [40].

Post-market surveillance
In the EU, as well as for other food products, the placing on the market of FS falls under the direct responsibility of the FBO, who is responsible for its safety. FBO is required to monitor the safety of products manufactured and placed on the market based on the evolution of scientific knowledge. In this regard, FBO is required to communicate to the competent authority any new data it knows about side or unexpected effects of the ingredients used in its products. However, the competent national authorities of the Member States can always carry out inspections and request information as part of the official control. Furthermore, at European level the Rapid Alert System for Food and Feed was established by Reg 178 2002 in the form of a network, to which the EC, EFSA and the EU Member States belong. The RASFF represents an effective tool that provides control authorities with a fast, efficient and European-wide mechanism, to exchange information on the measures adopted to guarantee food safety.
In the US the law includes a post-market inspection process for manufacturing sites to assess compliance with GMP and the reporting of potential serious adverse effects by FBO. In particular, FBO must submit all reports of significant adverse events linked to the usage of the DS to the FDA, no later than 15 business days after the report is received by the responsible person [29].

Discussion - Expert opinion

Both in the USA and the EU, FS and DS are governed by specific regulations to ensure their safety and quality. Both legislations do not require a market authorization for these food products but assign the responsibility to the FBO, to guarantee the safety of the FS/DS and ensure transparency in providing accurate information to citizens after the product is placed on the market. In particular, European FS and American DS facilities and products are subject respectively to state and federal post-market control and inspection. The definition of a FS/DS is overlapping since it is primarily considered a food product, regulated by a more general regulation applicable to all ordinary foods. Secondly, it is classified as a specific food intended to supplement the common diet, providing a concentrated source of nutrients. However, the regulatory approaches differ in some cases. In the USA, the legislation primarily focuses on compliance with labeling and production practices, as well as

post-marketing surveillance under the FD&C Act - section n. 201 regulation. On the other hand, in the EU, several regulations specifically govern FS. First, in the EU, the FBO is obliged to notify the FS to the competent authority of each individual member state where it sells the product. The competent authority may subsequently conduct checks on the products and their composition, also in collaboration with local health authorities. Moreover, unlike the FDA, which assesses only specific health claims before release the approval, the EU has issued a regulation on both nutritional and health claims; beyond that a specific regulation on novel ingredients defined as "novel foods", if they do not have a significant history of consumption in the EU before 1997. Both these regulations require authorization, based on scientific evidence available in the literature and in favor of food safety. In fact, in the EU, EFSA plays a unique role in providing scientific opinions at the community level to protect consumers in the consumption of FS, supporting the EC. Furthermore, significant progress has been made in the EU in listing permitted and employable substances in food through official lists, such as vitamins, minerals, and other substances. In some cases, these lists are based on specific risk assessments for certain ingredients conducted by individual member states. In the USA, there is no specific legislation governing the market entry of novel food ingredients and there is no list of permitted nutrients with corresponding daily dose limits. In fact, the NDI notification process is subject of a significant series of historic litigation without consistent enforcement, with the FDA conservatively estimating that as many as 3,500 NDI have not filed notifications under current law [41]. Draft regulations are currently pending to establish a temporary period of enforcement discretion to address the lack of enforcement of the NDI notifications.

Overall, the European legislative framework seems to have more specific regulations in favor of consumer safety than the American one. In particular, the absence of US market entry notification to regulators is perhaps the strongest point of contrast between the two systems. On the other hand, similar to European regulations, US ones also provide for serious safety assessment in relation to health claims that can be affixed to dietary supplement labels. The difference in market values between the two regions is well known, providing a comprehension of some less regulatory restrictions imposed on American food operators. However, it is noteworthy that consumer access to FS/DS is relatively unlimited in both markets, with a wide range of products available for purchase not only in traditional channels such as pharmacies, but also in supermarkets and online stores. Considering that FS/DS are not prescribed by general practitioners or physicians, and consumers have unrestricted access, it is crucial for both American and European citizens to be aware of the regulations, consciously read labels, and make informed choices when purchasing and using FS/DS. It is crucial for competent authorities in both regions to continue regular monitoring the application of existing food safety regulations by the FBO and to promote health care professionals' qualifications and training in the field to better assist their patients, to guarantee product quality in the market and protect consumer safety, respectively.

Conclusions

Food supplements are products increasingly occupying a significant market share in Western countries, contributing to meeting the nutritional and physiological needs of a large portion of the global population. The consumer's freedom of access to this market, as well as the wide variability of ingredients and substances contained in these products, necessarily focus on regulations that protect consumer safety in the DS use. The American and European markets are regulated by general and specific regulations, particularly in Europe, where several specific regulations govern this particular category of food, making it the region which currently has the most stringent regulations for this market worldwide. However, the responsibility still lies with the food business operator, who must ensure the safety of the marketed product and comply with applicable regulations. It is expected that more and more operators will launch new food supplements in Western markets. As a result, it is crucial for competent authorities in food safety to deepen and develop additional regulatory tools aimed to control the food supplement market, emphasizing the scientific evidence supporting the nutritional and health aspects, which ensure consumer safety when using these products, in protection of an increasing global market.

Contributions:

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Class of food derivates	European definition	European regulation	American definition	American regulation
Foods for specific groups (FSG): early childhood foods, foods for special medical purposes, foods presented as total dietary substitutes	Products intended for specific population groups with special nutritional needs, made nutritionally vulnerable by certain disorders or diseases	Regulation (EU) 609/2013	None specifically addressed	None specifically addressed
Infant formulas	Products expressly intended for infants (subjects younger than 12 months)	Regulation (EU) 2016/127	Infant formula is a food that may be the sole source of nutrition for infants (i.e., children up to 12 months of age) as an alternative to human milk.	FD&C Act section n. 412
Foods for special medical purposes / Medical foods	A food product expressly prepared or formulated and intended for the dietary management of patients, including infants, to be used under medical supervision	Regulation (EU) 2016/128	A food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements	Orphan Drug Act (section 5(b)(3))
Total dietary substitutes	Products that must provide a daily energy intake of between 600 and 1200 kcalories	Regulation (EU) 2017/1798	None specifically addressed	None specifically addressed
Gluten-free foods	Products specifically formulated for celiac people	Regulation (EU) 828/2014	Any foods that carry the label “gluten-free,” “no gluten,” “free of gluten,” or “without gluten” must contain less than 20 parts per million (ppm) of gluten.	Code of Federal Regulations (CFR) - Title 21, part 101

Foods with added vitamins and minerals/ fortified foods	Products where vitamins and minerals have been added voluntarily, in accordance with Regulation (EC) 1925/2006, which lists the list of permitted vitamins and minerals along with the list of their sources	Regulation (EC) 1925/2006	Food added with one or more vitamins or minerals or protein	Code of Federal Regulations Title 21 Part 104 Subpart B
Food supplements (FS)/ Dietary supplements (DS)	Food products intended to supplement the common diet and which are a concentrated source of nutrients, such as vitamins and minerals, or other substances having a nutritional or physiological effect	Directive 46/2002 (EC)	A dietary substance for use by man to supplement the diet by increasing the total dietary intake	Dietary Supplement Health and Education Act (DSHEA), 1994

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515 **Table 1.** Definitions of products under food regulations in the European Union and in the United States of
516 America.
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OBJECT OF THE REGULATION	EUROPEAN DEFINITION	EUROPEAN REGULATION	AMERICAN DEFINITION	AMERICAN REGULATION
Food / conventional food	General principles and requirements of food law	Regulation (EC) n. 178/2002	Articles used for food or drink for man or other animals, chewing gum, and articles used for components of any such article	Federal Food, Drug and Cosmetic Act 4, section 201 (FD&C Act)
Mandatory food information and labeling	Principles, requirements and responsibilities governing mandatory food information and food labeling	Regulation 1169/2011	Identity labeling of food in packaged form	Code of Federal Regulations Title 21 Part 101
Addition of vitamins and minerals and other substances to foods	Products where vitamins and minerals have been added voluntarily	Regulation (EC) 1925/2006	Products where vitamins or minerals or proteins have been added	Code of Federal Regulations Title 21 Part 104 Subpart B
Novel foods/new dietary ingredients	The ingredients in the FS and in all the foods without a significant history of consumption before May 15, 1997	Regulation (EU) 2015/2283	Ingredients that have been not marketed in the USA prior to October 15, 1994	Federal food, drug, and cosmetic act (FD&C Act), section n.201
Health and nutritional claims / Health claims, nutrient content claims, and structure/function claims.	*Nutritional Claims:* any indication which states, suggests or implies that a food owns particular beneficial nutritional properties *Health Claims:* any claim which states, suggests or implies the existence of a relationship between a specific food component and health	Regulation (EU) 1924/2006	• Health claims describe the relationship between a food substance and reduced risk of a disease or health-related condition • Nutrient Content Claims describe the level of a nutrient in a product • Structure/Function Claims describe the role of a nutrient or dietary ingredient in maintaining normal body structures or functions	1. 1990 Nutrition Labeling and Education Act (NLEA) 2. 1997 Food and Drug Administration Modernization Act (FDAMA) 3. Interim Procedures

Vitamins and minerals and their forms	Vitamins and minerals and their forms that may be added to foods and in particular to food supplements	Regulation (EC) 1170/2009	None specifically addressed	None specifically addressed

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521 **Table 2.** Regulatory framework concerning food supplements in the European Union and the Unites States of
522 America.
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