IJBPAS, October, 2023, 12(10): 4626-4640

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

COMPARATIVE REGULATORY ASPECTS ON NUTRACEUTICALS IN INDIA, JAPAN, EUROPE

R KAMARAJ* AND SHANKAR GANESH K

Department of Pharmaceutical Pharmaceutics, SRM College of Pharmacy, SRM Institute of Science and Technology, Kattankulathur-603203, Chengalpattu, Tamil Nadu, India

***Corresponding Author: Dr. R Kamaraj: E Mail: kamarajr@srmist.edu.in**

Received 20th July 2022; Revised 26th Sept. 2022; Accepted 9th Feb. 2023; Available online 1st Oct. 2023

https://doi.org/10.31032/IJBPAS/2023/12.10.7482

ABSTRACT

Dr. Stephen Defelice created the phrase "Nutraceutical" from the Nutrition & Pharmaceuticals at the year of 1989. The proposed definitions are derived as functional foods; dietary supplements; nutraceuticals. Nutraceuticals are the bioactive substances and components of dietary supplements, minerals, or herbs. In addition to basic nutritional value in foodstuffs, they are delivered as dosage formulations and are essential to the regular consumer's diet. In recent years there has been a growth of interest in nutraceuticals, which provided health benefits and are alternatives to modern medicines. A number of definitions and nomenclature for dietary supplementary exist worldwide; every country has its own guidelines and regulatory requirements which deal with the regulatory registration procedure of nutraceuticals. FSSA (Food Safety and Standard Authority) for India, FOSHU (Food for Specified Health Use) for Japan, and EFSA (European Food Safety Authority) for Europe. This review distinguishes the regulatory requirements for nutraceuticals in the above countries.

Keywords: Nutraceutical, Dietary supplements, FSSA, FOSHU, EFSA

INTRODUCTION

The phrase "nutraceutical" was developed in 1989 by Stephen De Felice, MD, the founder and executive director of the Foundation for Innovative Medicine, by combining the phrases "nutrition" and "pharmaceutical" (FIM). Nutraceuticals, as per DeFelice, seem

to be food products (or food components) that have medical benefits, such as their ability to prevent or treat disease. Food is crucial for human survival in order to maintain sustainable growth and combat disease. Nutraceuticals, functional foods, or dietary supplements are phrases used to characterize foods that promote health, regulate bodily biological functions, and aid in the treatment and/or prevention of pathological disorders **[1]**. However, there is no regulatory proposal to redefine functional foods and nutraceuticals using the term "nutraceutical" as it is frequently used in marketing. Food is referred to as "functional food" when it is prepared or cooked with "scientific intelligence," whether or not the user is aware of how or why the food is being used. As a result, functional food gives the body the proper balance of vitamins, lipids, proteins, carbs, and other nutrients for a healthy existence **[2]**. As a result, what one consumer perceives as a functional meal may be perceived by another as a nutraceutical. Citrus fruits and fortified dairy products (such as milk, yoghurt, paneer, etc.) are examples of nutraceuticals (e.g., orange, lemon, pomelos). The functional food industry and nutraceuticals are rising as a result of public interest and consumer demand, as well as ongoing research efforts to determine the qualities and prospective uses of nutraceutical compounds. Although there is little regulation of nutraceuticals in comparison to recurrent pharmaceuticals, their global prevalence is strikingly high. Major internet sellers sell nutraceuticals with therapeutic claims and swamp the market with them, all claiming to be of natural origin. At the nexus of nutrition and pharmaceuticals, nutraceuticals have the potential to offer new therapeutic avenues for the prevention of diseases connected to nutrition. Although there are countless opportunities for discovering nutraceuticals goods, the lack of regulation raises concerns about their safety. Rather than acting to protect the public's health, government agents just conduct surveillance **[3]**.

Consumer awareness of rising prescription prices, the ineffectiveness of conventional medications, or rising incidents of side effects has led to the rapid rise of nutraceuticals. The sizable elderly patient population, the growing emphasis on preventative medicine, insufficient current treatments for long-term conditions, conversations with healthcare providers that lack courtesy, and the trend toward using natural products for preventive and treatment, along with the demand for personalised medications. This transition has

been aided by the general public's belief that "natural is good." As a result, a sizable portion of the world's population, in particular in emerging countries like India, has high hopes for alternative medical care and nutraceuticals (including herbals and botanicals) **[4]**.

Numerous definitions and nomenclature for dietary supplements exist worldwide. In India, the term "nutritional" is known as "foods for special dietary uses". "Foods for special dietary uses or functional foods, or nutraceuticals or health supplements," according to the Food Safety and Standards Authority (FSSA). In Japan, there is Food for Specified Health Use (FOSHU). In Europe, we have the European Food Safety Authority (EFSA).

Nutraceutical factor

Their preferred organisational framework for nutraceuticals can vary depending on one's interests and/or educational background. For instance, nutraceuticals that are linked to lowering heart disease risk factors would be of particular interest to cardiologists. Specifically, they may be interested in compounds that are said to lower platelet-or free radical-dependent thrombotic activity as well as favourably affect hypertension and hypercholesterolemia. It would be especially interesting to study nutraceutical components like n-3 fatty acids, phytosterols, quercetin, and grape flavonoids. Meanwhile, drugs that target anticarcinogenic actions might be of greater interest to oncologists. These chemicals may enhance antioxidant and microsomal detoxification mechanisms, or they may inhibit the spread of cancer already present. Therefore, both chemoprevention and possibly adjunctive therapy may be of interest to them **[5]**.

Functional foods

A food can be rendered functional by using any technological or biological method to improve the bioavailability and increase the concentration of a certain component **[6]**. Consumers enthusiastically accept food products with health claims attesting to their functional potential to promote health, which goes beyond the provision of vital nutrients, and this is anticipated to lead to a drop in morbidity and mortality as well as an improvement in overall quality of life **[7]**.

India regulatory aspects of nutraceuticals

Nutraceuticals often fall under the functional food and dietary supplement categories. Numerous statutes have been passed for the purpose of controlling nutraceutical products. The President signed the Indian Food Safety and Standards Bill (FSSB) on August 23, 2006, after it was passed in 2005. The organization in place to regulate food and

nutrition is the Food Safety and Standards Authority of India (FSSAI). It is responsible for implementing the regulations governing the Indian market for dietary supplements. Nutraceutical foods are those that have been processed or created to meet specific dietary requirements, according to the FSSAI **[4]**.

Food safety and standards act

The Food Safety and Standards Act was adopted by the Indian Parliament in 2006 with the aim of unifying various current food laws under the control of one regulatory agency.

The Food Safety and Standards Act of 2006 contains eight legal systems:

- The Prevention of Food Adulteration Act of 1954
- The Fruit Products Order of 1955
- Meat and Food Products Order of 1973
- The Vegetable Oil Products (Control) Order of 1947
- Edible Oil Packaging (Regulation) Order of 1998
- Solvent Extracted Oil, De-oiled Meal, and Edible Flour (Control) Order of 1967
- Milk and Milk Products Order of 1992
- The Essential Commodities Act of 1955 Relating to Food

The Act offers necessary resolution to incorporate the idea of meals (foods with genetic modifications, healthy foods, nutraceuticals, and new foods) The Act provided for gaining a license to produce safe and high-quality food. This Act makes it possible to put into place a regulatory framework that is effective, transparent, and accountable **[1]**.

Product approval process in India

The FSSAI established a rule for the approval of unidentified foods on September 11, 2017. The following food products or food additives are covered by this regulation: Novel additions, contemporary preparation aids such as enzymes, and articles of food and food parts manufactured and isolated by microbes such as bacteria, yeast, fungi, or algae are all examples of modern food, novelty ingredients, even those handled utilizing technology **[1]**.

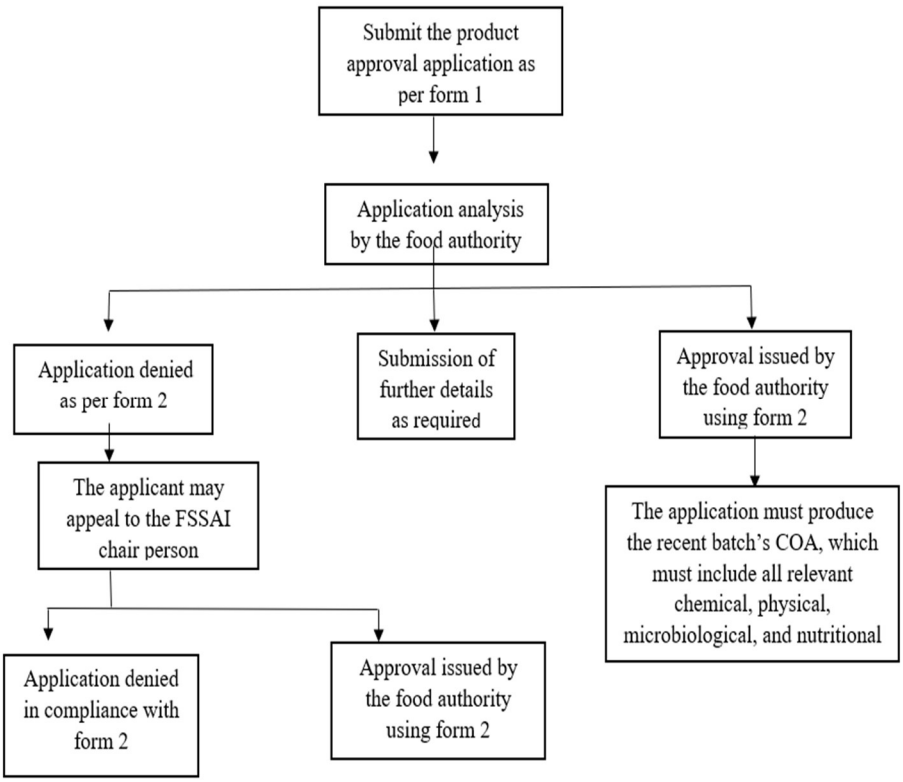

Figure 1: Product approval process in India

Licensing and registration requirements in India

• According to the procedure outlined in the 2011 FSSAI (licensing and registration of food businesses) rule, every operator of a food business in the nation must register and acquire a license.

- A manufacturer cannot start a firm unless they are registered or have a licence that is in good standing.
- Petty food producers must register with the commissioner and submit an application for a food license to the FSSAI office. Petty food producers are those with an annual turnover of less than Rs. 12 lacs.
- Before August 5, 2012, all current licences and registrations must be converted to FSSAI licences and registrations (now a couple months longer).
- Submit Form B of Schedule 2 to an authorised licencing agency to request a license. Within 60 days of the day the application ID number is issued, the license will be issued.
- After issuing the application ID number, the licencing authority can direct the food safety officer to

inspect a premises in compliance with these regulations.

- A license in format C must be issued by the licensing authority in accordance with these regulations' schedule 2.
- Any registration issued pursuant to the Regulations shall, unless otherwise specified, be valid and in effect for a minimum period of fifteen years.
- With the recent introduction of FSSA, India's nutraceutical regulation is evolving. It's possible that some of the information is contradictory, but this needs to be streamlined for the Indian business to take shape.
- While trying to get into the Indian nutritional field, it is crucial to concentrate on themes like product performance, product attributes study, getting authorization, and developing safety and labeling claims that are unique to India **[5]**.

Japan regulatory aspects of nutraceuticals

It is obvious how different pharmaceuticals and dietary habits are from each other. Unlike in the pharmaceutical category, which emphasizes substances that can cure or prevent illnesses, the diet food area was aimed at providing foods that had been improved or altered to provide nutritional benefits. "Health foods" describes two main subgroups. The first one includes elements that are known as "health foods," which can be a grey area related to unclear labelling standards and regulations. The heavily regulated field is Food with Health Claims (FHC), which is divided into three subdomains: Food for Specified Health Use (FOSHU), Food with Nutrient Function Claims (FNFC), and Food with Function Claims (FFC) (CAA Food Labeling, 2016) **[8]**.

Food for specified health use

In order to regulate and approve claims made about how food affects the human body, the Ministry of Health and Welfare (MHLW) developed the FOSHU framework in 1991. FOSHU is categorized in this regulatory framework as a specific food group that is sandwiched in between food and medication. In 1993, the first FOSHU goods were approved, which comprised low-phosphorus milk for patients and hypoallergenic rice. The aforementioned goods were eventually moved from the FOSHU category to a different category known as "food for illness," as medical claims are not permitted in FOSHU health claims to "prevent," "cure," and "treat" human disorders. The Japanese food sector has been compelled by the

FOSHU system to develop products that are functional, despite some early regulation mistakes. The Japanese Consumer Commission, Cabinet Office, has had control over the F0SHU system since 2009 **[9]**.

The four factors of FOSHU are: Regular/Ordinary, Qualified, Standardized, and Reduction of Disease Risk. Regular FOSHU has nutrients that seem to have a positive impact. To give the food producer the necessary market authorization and to confirm the scientific veracity of the particular health impact claimed for that FOSHU product, the Japanese government conducts a challenging and in-depth study. To make it easier for candidates to receive their Regular FOSHU approvals, the "Qualified FOSHU" and "Standardized FOSHU" categories were created. Foods with health functions that are sufficiently supported by scientific evidence are referred to as "Standardized FOSHU," whereas foods with health functions that are partially effectively supported by scientific evidence are referred to as "Qualified FOSHU." The foundations for its effectiveness are not always established. should be included in a qualified FOSHU. Only the "Reduction of Illness Risk FOSHU" kind of FOSHU is allowed to make claims about decreased disease risk on the label. A specific substance must have this impact confirmed clinically and nutritionally. Only two illness danger reduction claims were allowed, and they were: "Consuming the recommended quantity of folic acid, which is present in nutritious foods, may help women have safe pregnancies by lowering the chance of neural tube defects such as spondyloschisis during foetal development" and "Getting the right amount of calcium from nutritious meals may help young women's bones stay strong and lower their risk of developing osteoporosis as they age."

Food with nutrient function claims contains specific vitamins and minerals is labelled as such nutritional components' functions. Five minerals (calcium, zinc, magnesium, copper) and twelve vitamins make up these specialized nutrients (niacin, vitamin E, D, C, A, B12, B9, B6, B2, B1, panthotenic acid, biotin). The following are some examples of nutrient function claims: Fruit drinks with iron are important for the development of red blood cells, while vitamin E keeps cells healthy by preventing oxidation of body fat (in germ oil capsules). Food with nutrient function claims is exempt from the MHLW's pre-marketing approval process, unlike FOSHU products (such as the "Reduction of illness risk FOSHU") **[10]**.

Food with nutrient function claim

In order to comply with the "food with health claim" (FHC) system, criteria for FOSHU were incorporated in 2001. The MHLW introduced the FHC, a Japanese regulation system for health foods, in 2001. As of April 2001, it was divided into two types: FOSHU and FNFC. Functional claims for nutrients such as minerals, vitamins, and fatty acids are permitted under the current FNFC. Six minerals, including calcium, copper, iron, magnesium, potassium, and zinc, as well as thirteen vitamins, including vitamins A, B1, B2, B6, B12, C, D, E, and K, biotin, pantothenic acid, and folic acid, are currently approved for FNFC. Since 2015, the nutrient listings for FNFC now include unprocessed n-3 fatty acids. Because the advantages of consuming vitamins, minerals, and fatty acids have been shown via scientific research, labelling of the nutrients' functions is allowed. The normal daily dosage of each nutrient has been established using the maximum and minimum recommended intakes. Therefore, the amount of the nutrient in a FNFC product should fall between the specified higher and lower limits **[11]**.

Health claim in FOSHU

As of January 29, 2019, there were a total of 62 FOSHU goods that were approved. FOSHU product sales peaked at 6.2 billion dollars in 2007, but then fell slightly. According to half of the health claims, the GI tract's health could be improved with the help of probiotic lactobacilli, oligo-saccharides, and dietary fiber. Products with health claims for decreasing serum triglycerides made up roughly 20% of the total market. Twenty percent of the remaining claims were related to health issues such as high blood pressure, high LDL cholesterol, high blood sugar, tooth decay, and mineral uptake. We'll now explore the key active ingredients frequently found in these functional foods.

- Control of GI tract disorders: Of the health claims in FOSHU, 55% had to do with enhancing GI tract health. Yogurt and fermented dairy products that resemble yoghurt contain the majority of the probiotic microorganisms. Additionally, used for GI tract disorders are dietary fibre and oligo-sugar.
- Triglyceride decrease: A first classification of FOSHU was triglyceride reduction; the method allows use of a reduction in VLDL formation and an increase in its consumption in living organisms. Tea polyphenol and indigestible dextrin (dietary fiber) are commonly utilized in this field.

- Blood sugar levels FOSHU food contains indigestible dextrin to control blood sugar. By inhibiting the enzymes maltase and sucrase, dextrin can decrease the glucose absorption by the intestine. Guava polyphenol can also lower blood sugar levels by inhibiting amylase from performing its job.
- Blood pressure management: Cardiovascular illness is thought to be directly related to high blood pressure. A variety of antihypertensive peptides derived from food proteins were used to reduce high blood pressure. Most of these ACE-inhibitory peptides were found through proteolysis of fermentation and dietary protein sources **[12]**.

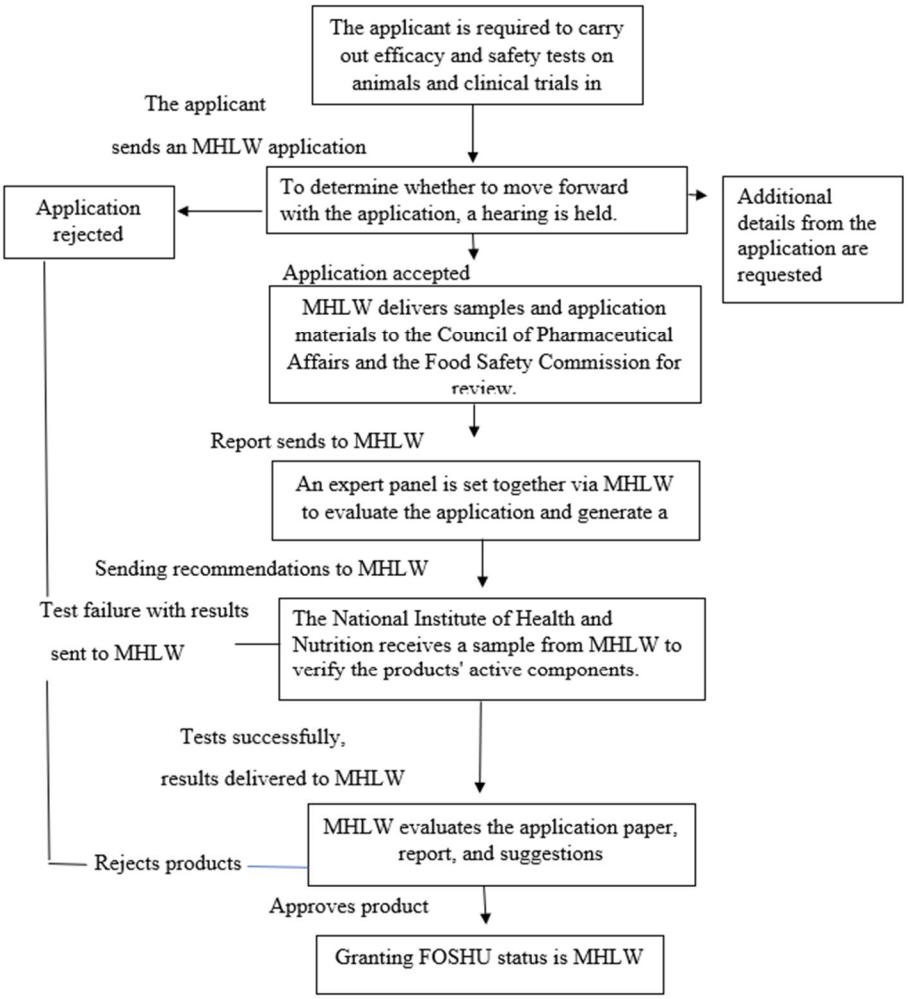

Figure 2: Registration process in Japan [13]

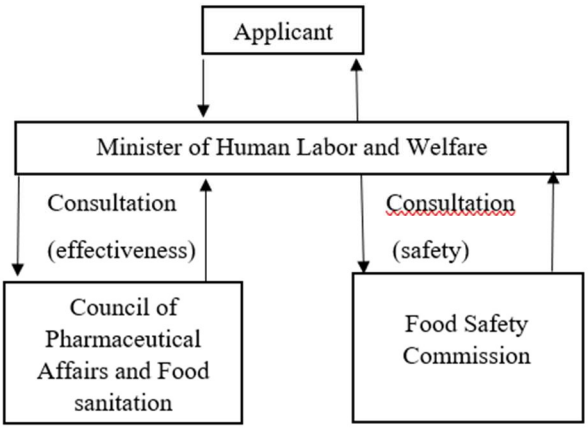

Figure 3: Approval process of FOSHU

Approval products of FOSHU

Specified Health Benefits Principal Ingredients

1. Foods related to blood pressure - Lactotripeptide, casein dodecapeptide, tochu glycoside, sardine peptide, etc.
2. Foods related to blood sugar levels - Indigestible dextrin, wheat albumin, guava tea polyphenol, L-arabinose, etc.
3. Foods related to blood cholesterol levels - Chitosan, soybean protein, and sodium alginate are degraded.
4. Foods related to dental hygiene - Paratinose, maltitiose, erythritol, etc.
5. Foods related to triacylglycerol - Middle chain fatty acids, etc.
6. Foods related to mineral absorption - Calcium citrate malate, casein phosphopeptide, heme iron, fracuto-oligosaccharide, etc.
7. Foods related to osteogenesis - Soybean isoflavone, basic protein from milk, and so on.

Requirements for FOSHU Approval

- There is clear evidence of effectiveness for the human body.
- There are no issues with safety (tests for animal toxicology, studies of the consequences of excessive intake, etc.).
- Making uses for nutrient-sound substances (e.g., no high sodium intake, etc.)
- Reputable quality assurance methods, such as product or ingredient requirements, manufacturing procedures, and analysis techniques, provide a guarantee that the product will be compatible with the product specifications at the time it is consumed **[14]**.

Europe regulatory aspects of nutraceuticals

The Dietary Supplement and Health Education Act (DSHEA, 1994), which was tried to be created in United States in 1994 and has since enabled a lot of flexibility and blurred the lines between foods and medications present in other nations, had such a significant effect on the early growth of nutraceutical ideas and goods. The DSHEA permits "an herbal or other biological" along with "a concentration, metabolite, constituent, extract, or combination of any component of the other divisions" to be found in dietary supplements. There are few requirements for this, so dietary supplements included a variety of phytonutrients or other substances that are classified as pharmaceuticals under the laws of most European countries. The liberal interpretation isn't one that the EU has adopted. The research for the European Commission was conducted by the European Association of the Self-Medication Industry (AESGP). It was discovered that several EU countries seemed to have difficulty uniformly applying the same laws across all pharmaceuticals. The "Herbal Medicinal Products" report revealed there was no similarity in the interpretation among the 15 European Union member states. Directive 65/65/EEC's provisions on herbs for medicinal purposes (AESGP, 1998). The difference between the herbage used for food and medication was noted **[15]**.

European law

Directives and regulations constitute the primary legislative acts of secondary European law. Imagine the many legal implications of rules and directives in order to comprehend how European law affects the legal systems of the EU member states. Quite precise restrictions are frequently found in regulations. They take effect immediately within the member states without the need for additional implementation of acts because they are self-executing within each of the member states. On the other hand, directives are typically less precise; they outline some aims and goals but leave it up to the individual member states to carry them out. By doing so, they grant member states some discretion over how precisely to incorporate their rules into their respective national legal systems. Indirectives must be carried out by the specific addressee member states in the case of small exceptional circumstances because they are not directly applicable within the member states **[16]**.

If a nutraceutical is offered with the aim of restoring, regulating, or changing individual

biological mechanisms, or if it is promoted for the treatment, diagnosis, or healing of a disease or illness, it is considered as a medication under the European Medicines Act.

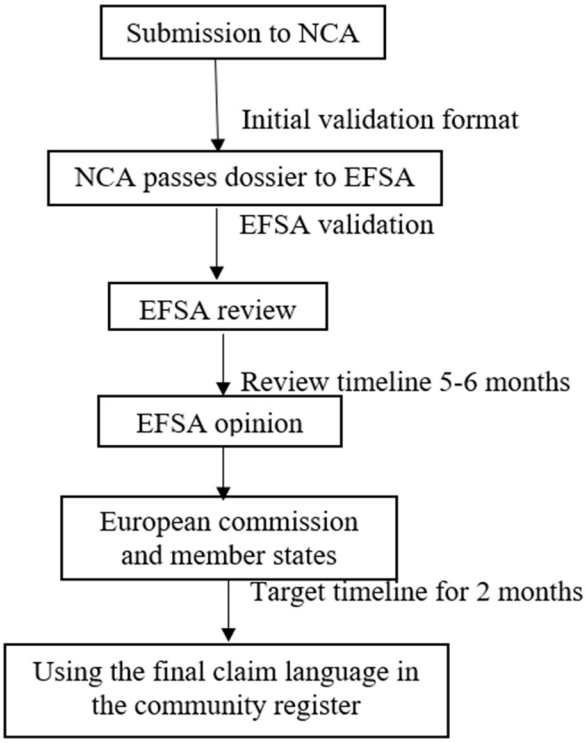

Figure 4: Approval process in European [17]

European labelling

A food's energy value, protein, carbohydrate, fat, dietary fiber, sodium content, or any minerals or vitamins listed in the directive's annex are all considered nutritional information and can be seen on the label. A nutrition statement is an assertion, implication, or hint that a food product possesses specific nutritional features relating to its energy content or nutrients (or categories of nutrients). Several examples include being high in protein, a natural source of calcium, light, low in fat, free of added sugar, and cholesterol.

Nutrition labelling regulations

The following statement on nutrition should be given on labels in one area, in one of two basic forms, and ideally like a table with the numbers allied: The energy values in calories as well as the milligrammes of protein, carbohydrate, and fat are included in class 1. Class 1 consists of Class 2 plus salt, fiber, carbs, and saturated fat, all measured in grammes. Class 1 format cannot be used if

any class 2 nutrient is claimed. Both classes can be expanded to include cholesterol, mono-unsaturated fats, poly-unsaturated fats, polyols, carbohydrates, and the vitamins and minerals specified in the Annex. The quantity of saturated should be included if any of the latter three are stated. Trans-fatty acids are subject to special regulations **[18]**.

Table 1: Comparative chart of India, Japan, and Europe

S.no	India	Japan	Europe
Definition	FSSA define Nutraceutical as "Foods for Special dietary use"	FOSHU defines Nutraceuticals as "foods with ingredients that have physiological effects on humans and are officially recognized as having health benefits"	ESFA defines Nutraceutical as "providing unbiased scientific guidance on the dangers of eating. and offers recommendations on current and potential food risks."
Regulations	FSSA (Food Safety and Standards Authority)	FOSHU (Food For Specified health use)	ESHA (European Food Safety Authority)
Regulations became effective in year	2011	1991	1994
Requirements for Registration under Regulation	A. Product evaluation B. Licenses C. Health & label claim	A. Clinical trail B. MHLW application C. Review & product verify D. Licensing & Claims	A. NCA submission B. EFSA review C. Final claim
Fees for registration	Rs. 100	1,600 $	Nil
Health claims	A. Nutrient function claim B. Other function claims C. Reduction of disease risk claims	A. Food with a health claim B. Food for special dietary uses	A. Nutrition B. Health claim C. Reduction of diseases' risk claim

CONCLUSION

Future medicines are being developed with the help of nutraceuticals, but their effectiveness, safety, and purity must be monitored. Therefore, it is crucial to adhere to the national regulatory framework when any new product or entry seeks to enter the nutraceutical industry of a given country. In this article, the registration process and approval process of nutraceuticals in India and Japan, European law and the approval process of nutraceuticals are explained. The laws governing dietary supplements in India, Japan, and Europe were compared.

ACKNOWLEDGEMENT

All the authors are appreciated for their contribution and synthesis of the manuscript.

CONFLICT OF INTERESTS

Authors declare no conflict of interest amongst themselves.

REFERENCE

[1] Kiran Bhupathiraju, *et al*., Regulations on nutraceuticals, functional foods, and dietary supplements in India, Nutraceutical and Functional Food Regulations in the United States and around the World, 445–464, 2019.

[2] Ekta K, Kalra, Nutraceutical-definition and introduction, AAPS Pharmsci, 5(3), 27–28, 2003.

[3] Jessica Blaze, A Comparison of Current Regulatory Frameworks for Nutraceuticals in Australia, Canada, Japan, and the United States, Innov pharm, 12(2), 2021.

[4] Ray, Arunabha, Regulatory Aspects of Nutraceuticals, Nutraceuticals, 941–946, 2016.

[5] Raj K. Keservani, *et al*., Nutraceutical and Functional Food as Future Food: A Review, Der Pharmacia Lettre, 2 (1), 106-116, 2010.

[6] M.B Roberfroid. What is beneficial for health? The concept of functional food, Food and Chemical Toxicology 37, 37(9-10), 1039-1041, 1999.

[7] Peter J. Jones, Stephanie Jew, Functional food development: concept to reality, Trends in Food Science & Technology 18, 18(7), 387–390, 2007.

[8] Mohamed Farid, Comparative Study of Functional Food Regulations in Japan and Globally, Global Journal of Health Science, 11, 6, 2019.

[9] Shimizu, Makoto, History and current status of functional food regulations in Japan, Nutraceutical and Functional Food Regulations in the United States and around the World, 337–344, 2019.

[10] Laura Dominguez Diaz, Virginia Fernandez-Ruiz, Montana Camara, An international regulatory review of food health-related claims in functional food products labeling, Journal of Functional Foods, 68, 103896, 2020.

[11] Shimizu, Makoto, History and current status of functional food regulations in Japan, Nutraceutical and Functional Food Regulations in the United States and around the World, 337–344, 2019.

[12] Iwatani, Shun, Yamamoto, *et al*., Functional food products in Japan, A review, Food Science and Human Wellness, 2019.

[13] Darshika Patel, Yvon Dufour, and Neil Domigan, Functional food and

nutraceutical registration process in Japan and China: Similarities and Differences, J Pharm Pharmaceut Sci, 11(4), 1-11, 2008.

[14] Food for Specified Health Uses (FOSHU), Retrieved from https://www.mhlw.go.jp/english/topics/foodsafety/fhc/02.html

[15] Om P. Gulati, Peter Berry Ottaway, Legislation relating to nutraceuticals in the European Union with a particular focus on botanical-sourced products, Toxicology, 221(1), 75-87, 2006.

[16] Konik, Ewa A, Jungling, Roman C, *et al*., Herbs and Dietary Supplements in the European Union: A Review of the Regulations with Special Focus on Germany and Poland, Journal of Dietary Supplements, 8(1), 43–57, 2011.

[17] Duttaroy, Asim K, Regulation of functional foods in European Union, Nutraceutical and Functional Food Regulations in the United States and around the World 2019, 267–276.

[18] J. Claude Cheftel, Food and nutrition labelling in the European Union, Food chemistry, 93(3), 531–550, 2005.