

# A Comparison of Current Regulatory Frameworks for Nutraceuticals in Australia, Canada, Japan, and the United States

Jessica Blaze, PharmD Candidate  
Nova Southeastern University

## Abstract

*The nutraceutical market is growing and the demand for products is increasing. Consumers are looking for cheaper alternatives to prescription medications as well as health products to supplement their dietary intake on a regular basis. Many countries classify these products into different categories based on their health claims. The purpose of this review is to compare and contrast the differences of regulatory frameworks in countries of similar status in regard to nutraceutical products: vitamins, minerals, herbal supplements, and probiotics. This review also takes into consideration the aspects of nutraceutical safety in relation to government regulations. It is evident that further discussion is indicated with regard to the harmonization of nutraceutical product regulation in a global context in order to promote and protect public health.*

*This literature review selected 27 documents for a review using a systematic search of internet databases and search engines including PUBMED and Google Scholar. These documents were reviewed and synthesized for data relating to nutraceutical regulation within the four different countries of focus. Outcomes included information on safety and toxicity, drug interactions, classification of products, and regulatory processes for nutraceutical product approval in each country.*

**Keywords:** Regulatory framework, regulation, nutraceuticals, Vitamins, minerals, Dietary supplements, Probiotics, Herbal supplements

## Introduction

### **What are nutraceuticals?**

In 1989, the term “nutraceuticals” was introduced by Dr. Stephen DeFelice meaning “food or part of a food that provides medical or health benefits, including the prevention and/or treatment of a disease.”<sup>1,2,3</sup> Although this definition may be accurate, it is currently not recognized by any regulatory authority in any country. In order to understand the complex meaning of nutraceuticals, people used to associate it with the Hippocratic principle “let food be they medicine, and medicine be they food”, which led to a broad misunderstanding that food and medicine are the same.<sup>3</sup> Today the regulatory definition of this term has not yet been finalized and is not well-established worldwide.<sup>1,4</sup>

All over the world, the nutraceutical market is rapidly growing, and regulations of nutraceuticals are continuously evolving without a clear regulatory definition.<sup>5</sup> Due to this ambiguity, nutraceuticals are not regulated as pharmaceutical products in certain countries but as food supplements.<sup>4</sup> In many countries, food supplements are consumed in order to complement the normal diet and ensure the proper intake of specific components (e.g., vitamins, minerals).<sup>3</sup> Many health conditions result in unique nutritional requirements and the need to

consume nutrients in nontraditional formats, so many physicians and consumers seek out nutraceutical products.<sup>6</sup> In many countries, nutraceuticals are commercialized to minimize the risk factors of various diseases.<sup>3,4</sup> One study in the United States showed that there is a role for the selected use of single and combined nutraceutical supplements, vitamins, and minerals in the treatment of hypertension as a complement to optimal nutrition and other lifestyle modifications.<sup>7</sup>

These products are often perceived as “safe” and less likely to have side effects. The scientific research on nutraceuticals and nutrition supplements is often misinterpreted or overstretched for commercial interests because of high consumer demands.<sup>8</sup> Within the last decade, consumers have increased their use of nutraceuticals to the point of intentionally avoiding pharmaceuticals and regarding prescription drugs as being unnecessary, too expensive, and sometimes unsafe.<sup>9</sup>

The use of nutraceuticals varies widely from country-to-country; nutraceutical use may be limited to general health and well-being while others permit use for medicinal purposes.<sup>5</sup> The global prevalence of nutraceuticals is noticeably high but has minimal regulation compared to traditional drugs.<sup>4</sup> The global market is flooded with nutraceuticals claiming to be of natural origin and sold with therapeutic claims by major online retailers. Nutraceuticals are at the interface between nutrition and pharma and have the capability of opening doors to seek new therapeutic alternatives for the prevention of nutrition-related diseases. Although, the possibilities are endless for the discovery of nutraceuticals products, their safety is at question

**Corresponding author:** Jessica Blaze, PharmD Candidate  
Nova Southeastern University  
College of Pharmacy  
David, FL  
Email: [jb4335@mynsu.nova.edu](mailto:jb4335@mynsu.nova.edu)

due to the lack of regulation. Governmental agents are only providing surveillance activity rather than intervening to protect public health.<sup>1</sup>

### **Safety and Toxicity**

The Manufacturing processes of nutraceuticals involves the use of solvents/additives, purification techniques, and storage conditions that may play a major role in the occurrence of contaminants, pesticides, and toxic chemicals in nutraceuticals.<sup>9</sup> Serious adverse effects of these products, including hepatotoxicity, renal failure, and carcinogenicity have been reported, so their safety has become an essential issue for regulatory authorities.<sup>5</sup> Pesticides are considered the most dangerous nutraceutical contaminants due to severe toxicity resulting from their ingestion.<sup>4</sup> Toxicity may vary from a mild skin rash to serious respiratory, neurological, and reproductive disorders. However, the use of pesticides is necessary to maintain the quality of medicinal herbs.<sup>4</sup> Other important contaminants of nutraceuticals are heavy metals, including lead, cadmium, mercury, and arsenic. The World Health Organization (WHO) has specified guidelines and limits for the presence of environmental contaminants, such as heavy metals in the final herbal product.<sup>10</sup> It is very important to define and implement rigorous, standardized manufacturing stages/procedures, quality assurance, and quality control techniques.<sup>9</sup>

### **Probiotics**

In recent literature, Probiotics have been classified as nutraceuticals. Probiotics are a new term that was originated from the phrase “for life”. The World Health Organization currently defines probiotics as “live microorganisms that when administered in adequate amounts confer a health benefit on the host”.<sup>11</sup>

The safety of foods or pharmaceuticals intended for human consumption, including probiotics, is important to consider in order to avoid health hazards. Some clinical studies confirmed that the safety of probiotics is apparent due to the absence of toxicity in diverse populations.<sup>11</sup> Many physicians and pharmacists recommend probiotics to patients without taking into consideration their true safety and efficacy from a pharmacological and toxicological perspective.<sup>11</sup> Probiotics are highly advertised, especially to consumers and patients who have difficulties distinguishing between high and poor-quality products. However, a recent review, concluded that probiotic use for some diseases lacks sufficient evidence, and more research is required to support probiotic recommendations.<sup>12</sup>

### **Herbal Medicines**

Herbal medicines are the products that consist of whole, fresh plant, or its parts, such as dried leaf, fruit, roots, or concentrated extracts.<sup>4</sup> To bring harmonization internationally, the World Health Organization considers herbal medicine to include herbs, herbal materials, and herbal preparations.<sup>5</sup> The herbal preparation could have active ingredients that are either part

of one plant or derived from the combination of multiple plants. However, some herbal medicine preparations at some countries contain active ingredients from non-plant sources as well, such as minerals or animal parts. Currently, there is an increasing number of consumers using herbal medicines to self-treat various medical conditions.<sup>5</sup>

The International Regulation Cooperation of Herbal Medicines (IRCH), a global network of regulating authorities responsible for regulating herbal medicines all over the world, hosts a meeting every few years. The purpose is to discuss the regulation of herbal medicine regulation in order to protect and promote public health. The last meeting was held in 2017 in involved governmental agencies from 22 countries, including Australia, Japan, Canada, and the U.S. This organization is largely supported by the World Health Organization.<sup>13</sup>

### **Drug interactions**

Recently, many studies have reported numerous nutraceutical drug interactions.<sup>4</sup> Some of the reported interactions could be serious and life-threatening. For example, aspirin and some non-steroidal anti-inflammatory drugs interact with herbal products containing ginkgo, turmeric, ginger, ginseng, chamomile and garlic. Consequently, these reported interactions increase the risk of bleeding due to the inhibition of platelet aggregation ability.<sup>4</sup>

### **Australia**

In Australia, Nutraceuticals fall under a broad category referred to as “Therapeutic Goods”, which are all regulated under the *Therapeutic Goods Act of 1989*. Within this category, there are medicines, biologics, and medical devices.<sup>14</sup> Complementary medicine is used as the regulatory term under the ‘medicine’ category which includes herbs, vitamins, minerals, and other nutritional supplements.<sup>5</sup> According to the TGA website, therapeutic goods can be very beneficial, but to be effective, they must modify the way the body works. Due to the many risks associated with this statement, therapeutic goods must be regulated in order to protect public health.<sup>5</sup>

Australia uses a high risk-based approach with a two-tiered system for the regulation of all medicines. Low-risk medicines may be listed on the Australian Register of Therapeutic Goods (ARTG), but high-risk medicines must be registered on the ARTG. High-risk medicines are required to be evaluated for their safety, efficacy, and quality. Medicines that are listed and not registered are not subject to this requirement.<sup>5</sup> For a low-risk medication to be listed, it can only contain low-risk ingredients in acceptable amounts, must be manufactured in accordance with the principles of Good Manufacturing Practice (GMP), and can only make indications for health maintenance and health enhancement, or certain indications for non-serious, self-limiting conditions.<sup>15</sup> The Australian Regulatory Guidelines for Complementary Medicines (ARGCM) provide in depth information about regulations and requirements for complementary medicines and also assist sponsors in meeting

their legislative obligations. High-risk medicines contain ingredients that require regulatory evaluation or make health claims regarding serious conditions.<sup>5</sup> As of October 2019, there are approximately 90,988 products in the Australian Register of Therapeutic Goods (ARTG) either listed or registered.<sup>16</sup>

### Canada

In Canada, both food and drug products are regulated by Health Canada with various directorates and branches overseeing specific product categories.<sup>17</sup> Nutraceuticals may be considered a food, a drug, or Natural Health Product (NHP) under the Canadian regulatory system.<sup>17</sup> The review focuses primarily on products that pertain to the NHP category. NHPs, also known as complementary medicines or traditional remedies are subject to the *Food and Drugs Act and Regulations*.<sup>18</sup> Natural Health Products Regulations came into effect on January 1, 2004 and Health Canada has since licensed over 43,000 products to be legally sold in Canada.<sup>19</sup> Natural Health Products include vitamins, minerals, herbal remedies, homeopathic medicines, traditional medicines such as traditional Chinese medicines, probiotics, and other products like amino acids and essential fatty acids. These products are restricted to oral, topical, or sublingual routes of administration.<sup>17</sup> NHPs must be safe to use as over-the-counter products and do not need a prescription to be sold.<sup>17</sup>

Natural Health products are under the authority of the Natural and Non-prescription Health Products Directorate (NNHPD).<sup>17</sup> NHPs are required to undergo a premarket approval process and to obtain license prior to entering the market. License submissions are reviewed by the NNHPD. This process requires applicants to describe the product ingredients (both medicinal and non-medicinal), its manufacturing process, and proposed claim as well as provide evidence detailing the product safety, efficacy, and quality.<sup>20</sup> Health Canada accepts varying types of evidence to support the safety and efficacy of NHPs, ranging from clinical trial data to references, published studies, journals, pharmacopeias, and traditional resources. The type and amount of supporting evidence required is dependent on the proposed health claim of the product and its overall risks.<sup>21</sup>

All manufacturers must obtain a site license to produce these products.<sup>20</sup> License holders are required to monitor all adverse reactions related to their product and must report serious adverse reactions to Health Canada.<sup>20</sup> Canada also has a post-approval safety surveillance authority, referred to as "The Marketed and Health Products Directorate (MHPD)". They work to assess signals and safety trends and risk communications concerning all regulated marketed health products, including NHPs. Health Canada also offers a "Licensed natural health products database" for consumers to check if a product has been licensed before use.<sup>20</sup>

### Japan

Japan categorizes nutraceuticals as "Foods in General" or "Food with Health Claims". Under the "Food with Health Claims,"

there are three distinct categories: (1) "Food with Nutrient Function Claims" (FNFC) that are mainly vitamins and minerals, (2) "Food for Specified Health Uses" (FOSHU) for other functions, and (3) "Foods with Function Claims" (FFC).<sup>5</sup>

The Ministry of Health, Labor, and Welfare is the main regulatory body for all drugs and health supplements.<sup>22</sup> The MHLW works to maintain strict regulations for medicines and food supplements.<sup>23</sup> Japan was the first country to regulate food supplements by issuing the Food for Specified Health Use (FOSHU).<sup>1</sup> It was introduced in 1991 as a regulatory system to approve statements concerning the effects of food on the human body.<sup>2</sup> Products bearing the FOSHU logo go through strict clinical testing and are allowed to make health claims on their labels because they are proven effective and safe for consumption as claimed.<sup>2</sup> Even if a health beneficial activity is not validated with scientific evidence, but the ingredient meets the safety requirements of FOSHU, it can be approved.<sup>1</sup> All substances designated as medicine are regulated under the pharmaceutical affairs act (1960 to the last amendment in 2013).<sup>3</sup>

In 2015, the category of "Foods with Function Claims" was introduced with the intention to categorize dietary supplements for health promotion and disease prevention separate from FOSHU. FFC products must be submitted to the Secretary-General of the Consumer Affairs Agency (CAA) for approval. Within this category, the government does not evaluate for safety and efficacy of functional claims. Businesses are required to submit a premarket notification and label their product in accordance with the Food Labeling Standards and "Guidelines on Notifications of Food with Function Claims". The FFC system has been able to accelerate the number of new entrants into the market, which has ultimately increased the growth of products within the market.<sup>24</sup>

Herbal medicine is regulated separately from "Food with Health Claims". Herbal medicines were developed in China and since have been used as crude medicines in both China and Japan.<sup>3</sup> It is now referred to as "Kampo Medicine" in Japan.<sup>5</sup> Products that fall into this category are classified as medicines instead of functional food and are considered to be the same as a government-regulated prescription drug. However, Japan does have over the counter Kampo medicines that must meet certain approval standards to be marketed. Currently, there are over 294 different formulas for approving OTC Kampo medicine products.<sup>5</sup>

### The United States of America

In the United States nutraceuticals are termed "Dietary Supplements".<sup>25</sup> In 1938, The Federal Food, Drug, and Cosmetic Act was passed and defined a dietary ingredient as "a vitamin, mineral, herb or other botanical, amino acid, or dietary substance for use by man to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of the preceding

substances".<sup>25</sup> The U.S. Dietary Supplement Health and Education Act (DSHEA) established the regulatory framework for dietary supplements as food through the Food and Drug Administration (FDA) in 1994.<sup>26</sup> DSHEA outlined the legal definition, labeling requirements, and process for adverse event reporting for dietary supplements. The definition of DSHEA: "*a product (other than tobacco) that is intended to supplement the diet that bears or contains one or more of the following dietary ingredients: A vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients*".<sup>4</sup>

The United States Food and Drug Administration (FDA) estimates that there are more than 85,000 dietary supplement products currently available in the U.S. alone.<sup>26</sup> According to the National Health and Nutrition Examination survey (NHANES) data, dietary supplements are widely used, with approximately half of U.S. adults and one-third of children reported using them.<sup>26</sup> Although their use has slightly declined over the years, multivitamin/mineral supplements (MVMs) are the most commonly used class of products, with approximately one-third of adults in the NHANES survey reporting their use.<sup>26</sup> Another study estimated that the number of Americans consuming dietary supplements on a regular basis to maintain or improve their health is over 158 million.<sup>9</sup>

Unlike the FDA's regulations of drugs, where safety and efficacy need to be proven before approval, dietary supplements are primarily regulated through post-market surveillance and are not approved at all.<sup>5</sup> The manufacturer is responsible for nutraceutical safety and neither FDA approval nor registration of the products is needed before sale.<sup>1,4</sup> The USFDA Modernization Act (1997) mentions that at least four months before a supplement is marketed, the FDA has to be notified about the health claims and/or the nutrient content claims on the product label of a dietary supplement which may be authorized by a statement of the Academy of Science or another federal body.<sup>2</sup>

A Dietary supplement must be intended for ingestion; therefore, cannot be indicated for use through any other means (e.g., applied topically, injected, inhaled, etc.).<sup>5</sup> According to FDA, the label of any nutraceuticals or dietary supplement products should state "*This statement has not been evaluated by the FDA. This product is not intended to prevent, cure or treat any disease*".<sup>4</sup>

All food supplement ingredients marketed before the implementation of DSHEA are considered safe and can be used however, those which were launched on the market after this date are considered novel ingredients and they have to be assessed by the FDA.<sup>3</sup> Dietary supplements may also not contain ingredients that were previously approved or studied

as drugs unless they were marketed as a dietary supplement prior to being approved as a drug.<sup>5</sup>

On February 11, 2019, the FDA held a Public Meeting to discuss responsible innovation in Dietary supplements. The purpose of the meeting was to hear suggestions from consumer health groups, industry trade associates, attorneys, physicians, and even representatives from regulatory agencies in other countries on how to modernize and reshape the FDA oversight of dietary supplements. During this meeting the FDA commissioner, Ned Sharpless made note to a new online tool referred to as the 'Dietary supplement Ingredient advisory list'. This is a new rapid response tool that will be used to alert the public when ingredients found in dietary supplements appear to be unlawful based on preliminary determination.<sup>27</sup>

Today many published research articles discuss the use of nutraceuticals for their different health-promoting disease-preventing effects, but there are several challenges associated with the development of nutraceuticals that are often ignored because of a lack of authoritative control. The Primary challenge in regulating dietary supplements is the lack of international consensus on how this category of products is defined; standards that ensure quality and integrity do not exist in a global context.<sup>26</sup> Overall, the Canadian regulations are the most rigid, and the United States regulations are the most flexible, with other countries falling in between.<sup>6</sup>

Despite regulations to improve the marketplace, many challenges remain; as a result, the quality and safety of products available can be highly variable, especially for herbal products. A need remains for continued efforts and improved techniques to assess the quality of dietary supplements, especially with regard to purity, bioavailability, and safety.<sup>26</sup> This review is intended to highlight and compare the regulatory framework of nutraceuticals, primarily focusing on vitamins, minerals, herbal supplements, and probiotics in four different countries: Australia, Canada, Japan, and the United States.

## Methods

One researcher independently conducted a literature search for regulatory guidelines of nutraceuticals pertaining to four different countries using the following electronic databases and search engines: PubMed (2019-2020), CINAHL via EBSCO (2019-2020), Google (2020) and Google Scholar (2020).

The initial screening included studies from 2019-2020. Google was used to find the regulatory/government websites for each country of study. Search term "regulatory website for [name of country]" was used. Each regulatory website included multiple articles of information for use. The use of google scholar allowed for a wide range of journals articles, reviews, documents, and books to be found. Search term "regulatory framework for nutraceuticals" was used on PubMed. "Nutraceutical regulation" was used as a search term on CINAHL via EBSCO. Google Scholar search terms were based on

each country of study. Search term “Regulatory framework for nutraceuticals in [country]” was used.

### Selection of studies

PubMed yielded 70 results (2001-2020) and was narrowed down to 13 results within 2019-2020. Five of these articles were accepted and eight were excluded. CINAHL via EBSCO presented more specific data pertaining to the nutraceuticals of focus and 80 results (1999-2020) were found then narrowed down to 20 results between 2019-2020. Two articles were accepted and 18 were excluded. Google Scholar yielded 968 results for The United States (2020), 550 results for Canada (2020); 730 results for Japan (2020); 504 results for Australia (2020).

The initial screening included title and abstracts of each document for areas of focus: vitamins, minerals, probiotics, herbal supplements, and regulatory guidelines in countries of focus. Excluded articles met most inclusion criteria but were ultimately excluded due to date range and not focusing on nutraceuticals or countries of study. Complementary searches were also conducted by screening the reference lists of retrieved articles to identify any other potentially relevant literature and were added to the reference list.

### Results

This literature search yielded 2,788 journal articles, reviews, books, and patents. After duplicates were removed 2,729 remained. 2,716 of these documents were excluded after being screened by title and abstract. 25 articles were assessed for eligibility and 7 were excluded due to study content. The screening process can be illustrated by **Figure 1**. 18 of the documents were found through the literature search 2 through complementary reference list search, and 7 through the various regulatory websites. Of the 27 documents included in this literature review, 5 emphasized safety and toxicity of nutraceuticals and drug interaction, 2 focused on probiotics, 3 referred to the use of herbal products, 5 focused on Australian regulation, 6 for Canada regulation, 7 for Japan regulation, and 7 dealt with the regulations of the United States.

After reviewing and synthesizing data, nutraceuticals of focus were classified based on regulatory category of each country for clarification (**Table 1**).

### Discussion

The current status of nutraceuticals in the global market can be seen as alarming. The chaos of regulation stems from the terminology and categorization, where these products are not considered medications. Many of these products are sold using the term “natural” and offering major therapeutic claims as a safe substitute to prescription medications. These products can also be easily bought from online retail stores without any regulations or controls. There is no uniform, consistent or standardized regulation governing the manufacturing, sales or marketing of any of these products.<sup>4</sup>

Regulatory bodies have the broad authority to legally stipulate what constitutes a nutraceutical, health claims, and manufacturing practices for these products. The ability of regulatory agencies to carry out this mission, however, is delayed by the large number of products and manufacturing facilities, as well as the low level of adverse event reporting.<sup>26</sup>

Current existing surveillance systems implemented in various countries provide useful information resources on the adverse events of nutraceuticals, including the FDA MedWatch program and Health Canada MHPD;<sup>5</sup> however, some countries still lack any sort of surveillance program. Establishing transparent analytical approaches with emerging technology will ensure worldwide quality and safety of dietary supplements and herbal products.

Precautions should be taken to reduce the risk of affecting human health. Despite major regulatory progress in recent years, a need remains for continued efforts and improved techniques to assess the quality of dietary supplements, especially with regard to purity and safety.

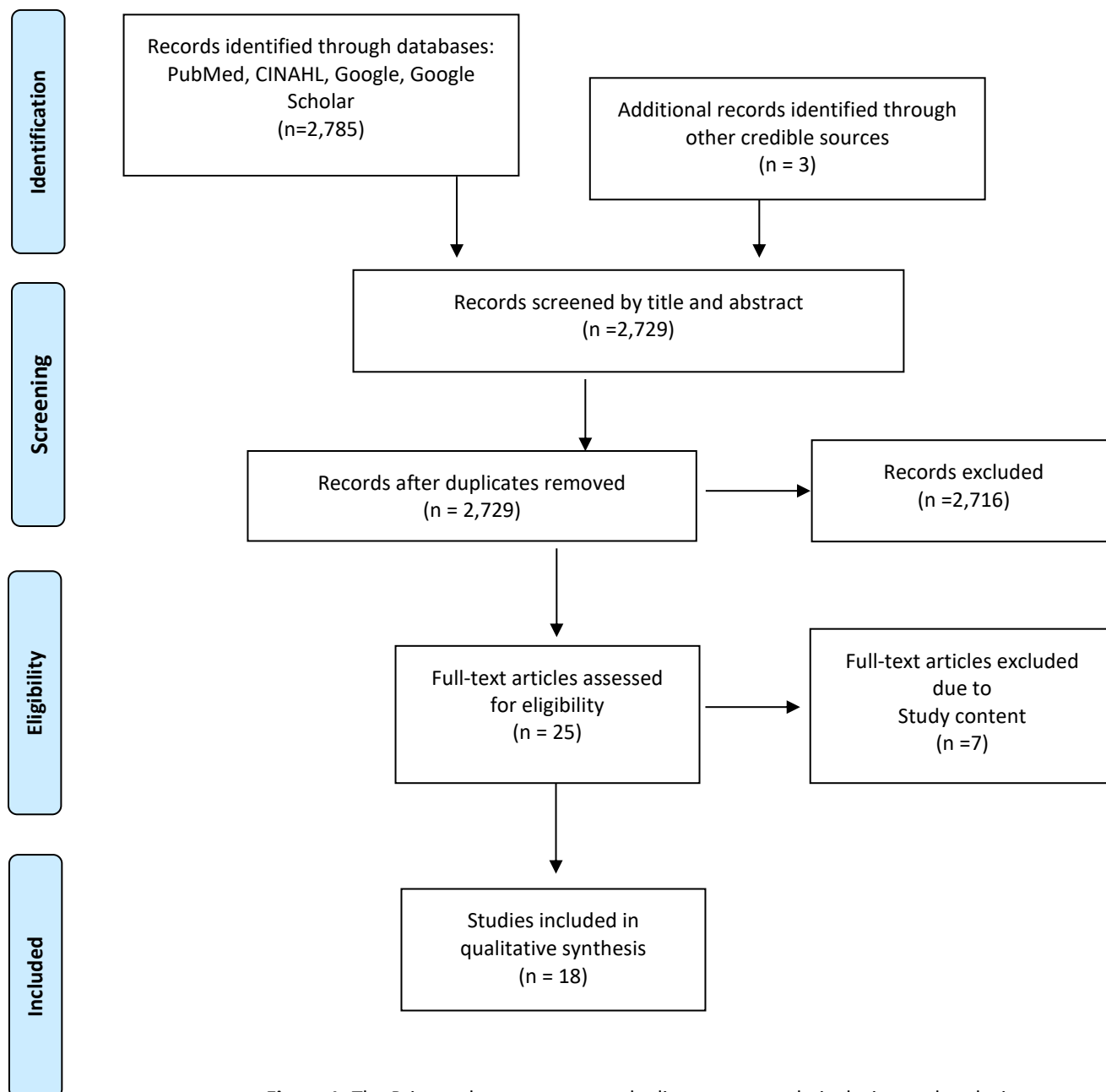
### Conclusion

It is evident that there is currently no harmonization between global regulatory markets in regard to nutraceutical classification and regulation. Due to the gap between increased usage of these products and lack of knowledge about their risks and benefits, it is important that global regulatory agencies discuss their regulatory principles in depth to understand the effect on public health. Although there is potential for emerging technologies to improve the harmonization of regulatory frameworks for nutraceuticals, further discussion and research must take place in order for this change to be enacted.

### References

1. Papetti A. Nutraceuticals: Health Benefits and Government Regulations. *Current Research in Nutrition & Food Science*. 2019;7(1): 1-4. Doi: 10.12944/CRNFSJ.7.1.01
2. Kapoor N, Jamwal VL, Shukla MR, Gandhi SG. The Rise of Nutraceuticals: Overview and Future. *Biotechnology Business - Concept to Deliver EcoProduction*. 2020; 67-92. Doi.org/10.1007/978-3-030-36130-3\_4
3. Domínguez Díaz L, Fernández-Ruiz V, Cámara M. The frontier between nutrition and pharma: The international regulatory framework of functional foods, food supplements and nutraceuticals. *Crit Rev Food Sci Nutr*. 2020;60(10):1738-1746. Doi: 10.1080/10408398.2019.1592107.
4. Helal NA, Eassa HA, Amer AM, Eltokhy MA, Edafiogho I, Nounou MI. Nutraceuticals' Novel Formulations: The Good, the Bad, the Unknown and Patents Involved. *Recent Pat Drug Deliv Formul*. 2019;13(2):105-156. Doi:10.2174/1872211313666190503112040

5. Thakkar S, Anklam E, Xu A, et al. Regulatory landscape of dietary supplements and herbal medicines from a global perspective. *Regul Toxicol Pharmacol*. 2020; 114:104647. Doi: 10.1016/j.yrtph.2020.104647.
6. Wiggins AKA, Grantham A, Anderson GH. Optimizing foods for special dietary use in Canada: key outcomes and recommendations from a tripartite workshop. *Appl Physiol Nutr Metab*. 2019 Nov;44(11):1258-1265. doi: 10.1139/apnm-2019-0013.
7. Houston MC. Treatment of Hypertension with Nutrition and Nutraceutical Supplements: Part 2. *Alternative & Complementary Therapies*. 2019;25(1): 23-36. Doi: 10.1089/act.2018.29197.mho
8. Siddiqui RA, Moghadasian MH, Nutraceuticals and Nutrition Supplements: Challenges and Opportunities. *Nutrients*. 2020;12(6): 1593.
9. Turner-Ravana, N. Nutraceutical and Functional Food Regulations in the United States and Around the World. *J Nutr Educ Be-hav*. 2020;52: 989 <https://doi.org/10.1016/j.tox.2006.01.001>
10. World Health Organization. WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues. 2007. pp. 1–35
11. Žuntar I, Petric Z, Bursac Kovačević D, Putnik P. Safety of Probiotics: Functional Fruit Beverages and Nutraceuticals. *Foods*. 2020;9(7): 947. Published 2020 Jul 17. doi:10.3390/foods9070947
12. Goldenberg JZ, Yap C, Lytvyn L, Lo CK, Beardsley J, Mertz D, Johnston BC. Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children. *Cochrane Database Syst Rev*. 2017 Dec 19;12(12):CD006095. Doi: 10.1002/14651858.CD006095.pub4.
13. World Health Organization. Essential medicines and health products. <https://www.who.int/medicines/areas/traditional/irc/h/en/>. Accessed December 1, 2020.
14. How therapeutic goods are regulated in Australia. Therapeutic Goods Administration, Australian Government Department of Health. <https://www.tga.gov.au/how-therapeutic-goods-are-regulated-australia>. Accessed December 1, 2020.
15. Listed Complementary Medicines. Therapeutic Goods Administration, Australian Government Department of Health. <https://www.tga.gov.au/listed-complementary-medicines>. Accessed December 1, 2020.
16. Australian Register of Therapeutic Goods. Therapeutics Goods Administration, Australian Government Department of Health. <https://www.tga.gov.au/australian-register-therapeutic-goods>. Accessed December 1, 2020.
17. Spagnuolo PA. *Nutraceuticals and Human Health: The Food-to-Supplement Paradigm*. London, UK: Royal Society of Chemistry; 2020.
18. Natural Health Products in Canada-A history. Health Canada. <https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription/regulation/history.html>. Accessed December 1, 2020.
19. Natural Health Products-Over 43,000 products authorized for sale and growing. Health Canada. <https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription/regulation/43-000-products-authorized-sale-growing.html>. Accessed December 1, 2020.
20. Drug and Health Products. Health Canada Web site. <https://www.hc-sc.gc.ca/dhp-mps/prodnatur/legislation/acts-lois/prodnatur/index-eng.php>. Accessed December 1, 2020.
21. Information Kit-Regulation for Natural Health Products. Health Canada. <https://www.canada.ca/en/health-canada/services/drugs-health-products/natural-non-prescription/regulation/information-kit.html>. Accessed December 1, 2020.
22. Food with Health Claims Food for Special Dietary Uses, and Nutrition Labeling. Ministry of Health, Labour and Welfare, Japan. <https://www.mhlw.go.jp/english/topics/foodsafety/fhc/>. Accessed December 1, 2020
23. Ismail SF, Daud M, Abd Ghani Azmi IM, Abd Jalil J. Enhancing Regulation of Nutraceutical Products in Malaysia: Lessons from Japan. *IJUM Law Journal*, 28((S1), 351–372. [https://doi.org/10.31436/iiumlj.v28i\(S1\).589](https://doi.org/10.31436/iiumlj.v28i(S1).589)
24. Sato K, Kodama K, Sengoku S. Corporate Characteristics and Adoption of Good Manufacturing Practice for Dietary Supplements in Japan. *Int. J. Environ. Res. Public Health* 2020;(17)13: 4748.
25. FDA Dietary supplements. Food and Drug Administration Web site. <https://www.fda.gov/food/dietary-supplements>. Accessed December 1, 2020.
26. Bailey RL. Current regulatory guidelines and resources to support research of dietary supplements in the United States. *Crit Rev Food Sci Nutr*. 2020;60(2):298-309. doi: 10.1080/10408398.2018.1524364.
27. Responsible Innovation in Dietary Supplements. FDA public meeting Transcript. <https://www.fda.gov/food/workshops-meetings-webinars-food-and-dietary-supplements/public-meeting-discuss-responsible-innovation-dietary-supplements>. Accessed December 1, 2020.



**Figure 1:** The Prisma above represents the literature search, inclusion and exclusion process of journal articles, reviews, books, and other documents.

**Table 1:** Classification of nutraceutical products for each country based on the governmental agency and the regulatory guidelines.

Table 1: Nutraceutical Classification			
Country	Regulatory Agency	Supplements	Medicines
Australia	Therapeutic Goods Administration (TGA)		"Complementary Medicines" •Herbs •Vitamins •Minerals •Nutritional supplements •Homeopathic medicines
Canada	Health Canada (HC)		"Natural Health Products" •Vitamins •Minerals •Herbal remedies •Homeopathic medicines •Traditional medicines (e.g., Traditional Chinese Medicine) •Probiotics
Japan	Ministry of Health, Labor, and Welfare (MHLW) Consumer Affairs Agency (CAA) for supplements	"Health Foods"	"Kampo Medicine"
United States	Food and Drug Administration (FDA)	"Dietary supplements" •Herbs •Vitamins •Minerals •Amino Acids •Dietary substance used to increase daily total intake •concentrate, metabolite, extract, or combination	