REGULATION OF FOOD SUPPLEMENTS (VITAMINS AND MINERALS) IN EU, US, AND THAILAND: A COMPARATIVE STUDY

Ms. Jarunee Intrasook 791016383040

MSc. Thesis (LAW-80436)

Supervisor: Prof. Dr. Bernd van der Meulen

Law and governance group, Social sciences

Wageningen University and Research Centre

FEBRUARY 2013

Regulation of food supplements (vitamins and minerals) in EU, US, and Thailand: A comparative study

Name: Jarunee Intrasook

Reg. No.: 791016383040

Programme: MSc. Food Safety

Course: Thesis Law and Governance (LAW – 80436)

Supervisor: Prof. Dr. Bernd van der Meulen

Law and governance group, Social sciences

Wageningen University and Research Centre

February 28, 2013

ABSTRACT

Food supplements or dietary supplements are food products containing single or combinations of micronutrients (vitamins and minerals), or other substances in a dose or concentrated form, and consumed in a small unit of quantities to supplement a normal human diet with benefits of health promotion, nutritional or physiological effects. Food supplements are sold worldwide, especially the micronutrient supplements because consumers use them to treat nutrition deficiencies, sustain life, and avoid costly disease treatments. However, there are some problems from supplement consumption resulting in consumer health effects. An international organisation like the CAC, therefore, adopted the codex guidelines on vitamin and mineral supplements in 2005 and disseminated all WTO members including EU, US, and Thailand to conform or harmonise into their national regulations. Objectives of this study are to acquire knowledge of regulatory systems of food supplements in EU, US, and Thailand and to propose recommendations for strengthening the regulatory system in Thailand by the comparative study among three countries.

This comparative study shows that national regulations in EU, US, and Thailand including control measures of pre- and post-market systems have been comprehensively enforced under 3Ps perspectives (**P**roduct, **P**remises, **P**resentation) by conforming to the Codex guidelines. There are both similar and different measures implemented depending on national consumption data, available scientific information, and other factors, particularly economic and social issues. In the viewpoint of consumer protection, the EU regulatory system is the most effective since several requirements and activities are legally applied, however, main drawbacks are time-consuming and limitation of product development. In contrast, the US system is more flexible and industry friendly resulting in enhancing product development and availability for consumer choices. It also supports the US to have the biggest market share of supplement products in the world; however, major problems on insufficient scientific information and inactive communication network are huge obstacles for rapid response on non-compliant supplements. In Thailand, many measures on pre- and post-market controls have been enforced but the system should be improved for more effectiveness of consumer protection and increase in fair trade facilitation.

Recommendations proposed for improving the Thailand system are to increase resources for scientific data, develop a specific hygiene and quality system for food supplements, establish an integrated control plan for the national monitoring, strengthen active communication and information exchange among stakeholders, enhance knowledge of officers, food business and consumers, improve other supportive measures such as an independent risk assessment body and a traceability system, as well as more researches on other substances, especially in botanical ingredients for an appropriate risk management.

Keywords: food supplements, dietary supplements, regulation, EU, US, Thailand, pre-market control system, post-market control system

ACKNOWLEDGEMENTS

It is a pleasure to thank all people who have contributed to this thesis. First and foremost I would like to express my gratitude to my thesis supervisor, Prof. Dr. Bernd van der Meulen for his constant support, sound advice, and lots of comprehensive ideas during the course of this work. Thank you Prof. Harry Bremmers for his contribution in my thesis defence.

I would like to give my sincere thanks to Dr.Tipvon Parinyasiri, the director of Bureau of Food, Thai FDA giving me an opportunity to study the MSc. Food Safety programme that opens up my world to a great food safety system in Europe and new experience for my life. Moreover, I am grateful to all colleagues of the Bureau of Food for their advice on the topic and valuable information to make this thesis possible. I also would like to acknowledge the Royal Thai Government for providing me financial support during my whole academic years.

I will forever be thankful to all of Thai community in Wageningen giving me warm welcome, generous care, and all helps that make my life here easy. Special thanks to P'Good and P'Aom, my big sponsors for free coffee ☺, as well as to my G-gang members; Paul, Ham, Pear, and Jan for the enjoyable time we spent together, and I hope that our contract has been continued.

I am indebted to all international friends, especially Thushara, Tomoko, Patricia, Dasep, Jambay, Hussain, and Rashida for warm friendship, moral support and motivation. I am also thankful to all Thai friends for their help on reading and correcting my thesis with spiritual support. I find myself lucky to have friends like them in my life.

Last but not least, I would like to express the profound gratitude to my beloved family for supporting me throughout my entire life. Without their love and encouragement, I would not have finished this thesis.

"Each morning we are born again. What we do today is what matters most."

-Buddha-

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

ACCSQ-TMHS	ASEAN Consultative Committee on Standard and Quality for Traditional Medicine and Health Supplement
ASAI	Advertising Standards Authority for Ireland
CAC	Codex Alimentarius Commission
CCFH	Codex Committee on Food Hygiene
CCFL	Codex Committee on Food Labelling
CCGP	Codex Committee on General Principles
CCNFSDU	Codex Committee on Nutrition and Foods for Special Dietary Uses
CFSAN	FDA's Centre for Food Safety and Applied Nutrition
EC	European Commission
EFSA	European Food Safety Authority
EU	European Union
FAO	Food and Agriculture Organisation
FBO(s)	Food Business Operator(s)
FSAI	Food Safety Authority of Ireland
FVO	Food and Veterinary Office
GMP	Good Manufacturing Practice
HACCP	Hazard Analysis and Critical Control Point
HHS	The U.S. Department of Health & Human Services
ISO	International Organisation for Standardisation
MoPH	Ministry of Public Health of Thailand
MS(s)	Member State(s)
ODS	Office of Dietary Supplements
RASFF	Rapid Alert System for Food and Feed
SPS	Sanitary and Phytosanitary
Thai FDA	Food and Drug Administration of Thailand

UK	United Kingdom
UN	United Nation
US	The United State of America
U.S. FDA	The United State Food and Drug Administration
WHO	World Health Organisation
WTO	World Trade Organisation

1. INTRODUCTION

1.1 Research background and problem statement

Food supplements called in EU[1] or Dietary supplements, officially called in US (U. S. FDA, 1994)[2] and Thailand (ACCSQ-TMHS, 2006)[3] are classified as food products containing micronutrients and intending to supply the normal diet. Demand of supplements, used as a general term in this thesis, has been increased because of changing consumer behaviour patterns (Greger, 2001).

Recently, consumer awareness on health continuously increases in line with availability of health information going hand in hand with the aging of populations and increasing risk for lifestyle diseases (Kearney, 2010). The relationship between disease and diet has most been discussed. Also, many scientific researchers have supported that the dietary imbalance is one major risk factor relating to food consumption. In particular micronutrients such as vitamins and minerals are significantly required in small amounts for human development, maintenance, and effective functions, imbalance of these nutrients leads to long-term diseases such as cancer and cardio-vascular disease (Hanekamp & Bast, 2007). Therefore, healthy food trend has universally increased, especially in food supplements. The use of supplements is widely common in the general population and athletes in EU, for examples, 47% of German women and 41% of German men regularly take supplements consisting of vitamins, minerals, and their combinations which are the outstanding product comparing to other supplements (Reinert, Rohrmann, Becker, & Linseisen, 2007). From a national survey, both Danish females and males commonly use micronutrient supplements approximately 60% and 51% of interviewed participants, respectively (Tetens et al., 2011). Consumption survey on dietary supplements in US between 2003 and 2006 has indicated that 49% of the US population (44% of males and 53% of females) take this product and approximately 30% of the surveyed population employs multi-vitamin and multi-mineral supplements containing vitamin B_6,B_{12}, C, A, and E while 26-27% of the population use zinc-, and magnesium containing-supplements (Aoude P., 2012). In Asian countries, the trend of supplement consumption also significantly increases, e.g., the use of multivitamins and minerals supplements has increased from 23.2% in 1993-1996 to 35.8% in 2005-2008 based on the Nutrition and Health survey in Taiwan (Lin, Lin, Kao, Yang, & Pan, 2011). In Thailand a trend of domestic consumption of imported food supplements between 2001 and 2005 increased approximately 13% (Arunanondchai J., 2007). A change of this consumption pattern in worldwide level results in enhancing global markets on the food supplements. According to the global market research in 2010 (Analytics, 2012), US was the largest world market for nutritional supplements which include vitamins, minerals, herbs, and other supplements related to boost the nutritional content of the diet. Western Europe and Japan were the next large markets of the nutritional supplement products, respectively. The nutritional supplement market can be divided into various segments, namely vitamins, herbal supplements, sport nutrition, minerals, meal replacement supplements, and specialty supplements. In 2010, the vitamins segment recorded highest sales compared to other segments. A research report of global vitamin and supplement market (Reportlinker, 2010) indicated the US was also the world leader in terms of market share with around 30% of worldwide market, or $20 billion. The second biggest market share was Japan with approximately 22% of the world market or over

[1] Article 2(a) of the Directive 2002/46/EC
[2] Section 3 (a) of the DSHEA of 1994
[3] ACCSQ TMHS, 2006, p. 4

$15 billion while Europe had a 14% share of the worldwide market in vitamins and supplements. In the EU market, vitamins and minerals also had the largest share (50-55%) of the food supplements at retail level in 2009 (Brookes, 2010). In Thailand, based on collected data in 2005 (Arunanondchai J., 2007), 40 percent of dietary supplements consumed in national level are imported, especially from US. Other exporting countries are such as Ireland, France, Switzerland, Japan, Netherlands, Germany and Australia, whereas Japan, Philippines, Singapore and Vietnam are major countries exporting raw materials into Thailand for further production.

Because of this rapid increase in use of food supplements in the nationwide level, especially vitamins and minerals helping to sustain life and inexpensively treat nutritional deficiencies, many research studies (Havel, 1999; Lichtenstein A.H. , 2005) discussed the general issues of abuse of supplements, food, and drug from consumer perception and consumption. Major reasons resulting in confusion of usage of supplements are not only because the products are produced in forms which are similar to drugs and, but they are neither drug nor hormone based product. Consumers do not have enough nutrient information or lack or insufficient knowledge about supplements (Hanekamp & Bast, 2007) whereas incorrect and misleading information, especially in nutrition and health claims, is frequently found on product labels and advertisements (Coppens, Da Silva, & Pettman, 2006). To avoid this misleading and to ensure that food supplements are safe for consumer health, relevant regulations have been established including labelling and claiming in order that the food business operators (FBOs)[4] provide correct and clear information to consumers without misleading to medical therapy (Eberhardie, 2007). At the international level, food standards and guidelines called Codex Alimentarius related to food supplements such as "Guidelines for vitamins and mineral food supplements; CAC/GL 55-2005" have been developed to support trade facilitation and consumer health protection for all WTO members (Dumoff, 2004). Because the Codex Alimentarius is a set of non-legally binding standards, several countries provide deviating regulations based on their own scientific assessments. In addition, specific requirements on pre-market approval of food supplements as well as other food control measures such as precautionary and post-market control activities by food safety authorities have been established in order to evaluate safety aspects of these products and enhance consumer confidence in controlling these food supplements (Schwitters et al., 2007). By these differential laws between countries and various competent agencies involved with international trade in food supplements can be confronted. An exporting country may not be able to follow all requirements of the importing country due to lack of up-to-date information, insufficient knowledge and technology including budget to develop the product for further compliance. Moreover, a stricter rule of one country than other leads to an international trade obstruction (Yeung, Hobbs, & Kerr, 2006).

Apart from the problem of international trade obstruction, difficulties on controlling food supplements in a territory also arise. For example, in 2008, U.S. FDA received 596 reports of serious adverse events and 352 voluntary reports of moderate or mild adverse events which related to dietary supplements resulting from the increasing market of dietary supplements in US from 4000 in 1994 to approximately 75,000 products in 2008 (Marcus & Grollman, 2012). Confusion of legal interpretation of the definitions of food supplements and other similar products like medicinal products is one example of problems resulting in failure of legal implementation between Community and national laws in the EU (Krutmann, Humbert,

[4] FBOs refer to a responsible person on the food supplement business under the food law. This word is legally used in the EC laws, but it is also generally used in this study for regulations of US and Thailand with the same definition.

Karajiannis, & Fish, 2011). Moreover, some food supplements provide little or no information about side effects or interaction with other nutrients leading to damage the consumer health (Petroczi, Taylor, & Naughton, 2011). Similar to EU, a large proportion of the food supplement in Thailand is through internet and direct sale often by companies registered outside the country and reach products directly to consumers where they are not subjected to check on legal compliance. From 1st to 31stAugust 2012, the Thai FDA received 125 complaints from consumers and the most issues were related to food supplements because they reached consumers without pre-market authorisation and non-compliance with relevant safety requirements such as unsafe substances found in the products. Besides, a result from post-market surveillance in the same month, especially in advisements through websites indicated that major problems from food supplements were caused by misleading information, unauthorised health claims related to disease treatment, weight loss, or sex drive increases, particularly from imported products which are widely distributed via social media and websites (FDA., 2011)[5]. Some of these products often was not able to be traceable to the producers or manufacturer due to false information as well as the traceability system in Thailand was implemented based on voluntary measures while responsibilities of product withdraw and/or recall were mainly taken by competent authorities. Apart from problems of food supplements relevant with safety and advertisement aspects, consumers were also one of factors influencing problems on food supplements since they mostly had inadequate knowledge to choose safe and authorised food supplements affecting to their health. Recently, Thai people have changed lifestyle, especially in consumption behaviour to have more healthy life by eating healthy food and food supplements but less exercise. Most of people believe in benefits from properties of food supplement which are often over claimed as well as the food supplements can be easily reached to consumers via direct sale and websites so that the products have been widely spread to many local areas and have been consumed much more than necessary for consumer health (FDA.)[6].

Therefore, appropriate and necessary regulations and legal actions relevant with food supplements to protect consumer health as well as facilitate food business operators are highly challenging to competent authorities of each country, particularly in Thailand to have more effective regulations and appropriate enforcement based on up-to-date scientific evidences as well as effective measures enforced in other countries like EU and US.

1.2 Research objectives

Main objectives for this thesis research are to

1.2.1 Acquire knowledge of regulations and enforcement system of food supplements focusing on vitamins and minerals in EU, US, and Thailand comparing with Codex standards.

1.2.2 Propose recommendations to strengthen the regulation and control system in Thailand based on the comparative analysis of these three countries for enhancing consumer protection, reducing limitations, and supporting trade facilitations.

[5] Thai FDA, Public and Consumer Affairs Division, 2012
[6] Thai FDA, Digital library.

1.3 Research questions

The thesis research will provide answers for the following research questions:

1.3.1 What are regulations of food supplements in EU, US and Thailand?

1.3.2 How are the food supplements controlled before and after placing on market?

1.3.3 What are similar and different measures based on regulations and control system of food supplements in Codex guidelines, EU, US and Thailand?

1.3.4 In what way can regulatory system on food supplements in Thailand be strengthened?

1.4 Methodology

In order to understand regulations and controlling measures regarding food supplements focusing on vitamins and minerals from EU, US and Thailand, a legal research method is applied, consisting of a systematic review of legal document, policy documents and secondary literature. From collected data, all information on regulations and measures taken from EU, US and Thailand is analysed and compared as a basis to propose some recommendations for reinforcing the regulatory control of food supplement products.

1.5 Thesis outline

This thesis consists of six chapters. A scope of this thesis, methodology and outline are described under the first chapter. In chapter 2, general information on relevant authorities and their responsibilities to control food supplements from an international basis as the CAC to regional and national areas, particularly in EU, US and Thailand is presented. The third chapter elucidates about regulations including definitions and safety requirements for pre-market authorisation of food supplements including production control, labelling, and claims from EU, US and Thailand. The next chapter focuses on activities for post-market control systems such as sampling and enforcement, monitoring and surveillance programmes, communication and information exchange, including empowerment and education for relevant stakeholders. The fifth chapter discusses similarities and differences of regulations based on international guidelines and control systems of food supplements in EU, US, and Thailand, and then the last chapter presents conclusions and some recommendations to strengthen the effective regulatory system of food supplements in Thailand.

2. ORGANISATIONS RELATED TO FOOD SUPPLEMENTS

This chapter briefly provides information on organisations responsible for controlling foods including food supplements. The CAC is an international organisation working to develop food standards, guidelines, or recommendations on food safety under WTO and SPS agreements for protecting consumers and facilitating fair trade among WTO members. In general, the organisations in US, EU, and Thailand are arranged to control safety of foods including food supplements based on the risk analysis principle. Competent authorities are assigned for risk assessment and risk management while the communication tools are regularly used for the risk communication among stakeholders at all stages the food chain. However, they are differentially based on political and managerial systems of each country. In EU, EC adopted a fundamental system at the regional level while all MSs shall bring into force the national regulations with additional rules as necessary. In addition, the independent EFSA and the FVO support the effectively controlling system for EC and MSs to achieve a high level of consumer protection. Several agencies are also involved in food safety management in US but there is one major regulation on dietary supplements directly applied into both federal and state levels as similar as the system in Thailand.

However there are different systems with various agencies involved in regulating and controlling food supplements. The main objective is mostly similar in EU, US, and Thailand by protecting their consumer health based on risk analysis and scientific evaluation to ensure the supplements placed on the market are not harmful and mislead to consumers.

2.1 CAC

The CAC created in 1963 by the FAO and WHO under the UN is an international intergovernmental body responsible for implementing the Joint FAO/WHO Food Standards Programme(FAO/WHO, 2006b). The main objectives of this establishment are to protect consumer health and ensure fair trade facilitation in international markets of food through the development of Codex Alimentarius – a collection of food standards, guidelines, codes of practices, and other recommendations relating to foods, their production, and food safety (Zlotkin, Siekmann, Lartey, & Yang, 2010). Recently, there are 185 members consisting of 184 member countries and 1 member organisation (EU), and 211 Observers (48 intergovernmental organisations, 147 non-governmental organisations, and 16 UN organisations)(Codex, 2012a) coordinating closely to develop these food standard works. US and Thailand have been a member of CAC since 1963 while EU has become an organisation member since 2003 (FAO/WHO, 2011)[7]. The CAC meets every two years, alternatively at FAO headquarters in Rome and at WHO headquarter in Geneva for plenary discussion and adoption of food standards. The process of codex standard development consists of 5 to 8 steps that takes years to complete the final draft and submit to the CAC meeting (Dumoff, 2004). Once the draft standard is adopted by the CAC, it is published and added to the Codex Alimentarius (FAO/WHO, 2006b).

Under the Rules of Procedure of the CAC, the commission is empowered to establish subsidiary bodies – Codex Committees and Coordinating Committees in order to continuously prepare and update food standards and related texts to approach the tasks of the CAC based on current scientific evidences,

[7] FAO and WHO, 2011,p. 194-195

technology of food production and needs of the member countries. Codex committees were established specially regarding specific topics such as Food Contaminants, Food Labelling, Food Hygiene, Pesticide Residues, and Food Additives (Codex, 2012a). They annually meet to develop food standards, guidelines, or recommendations relating to their tasks and responsibilities.

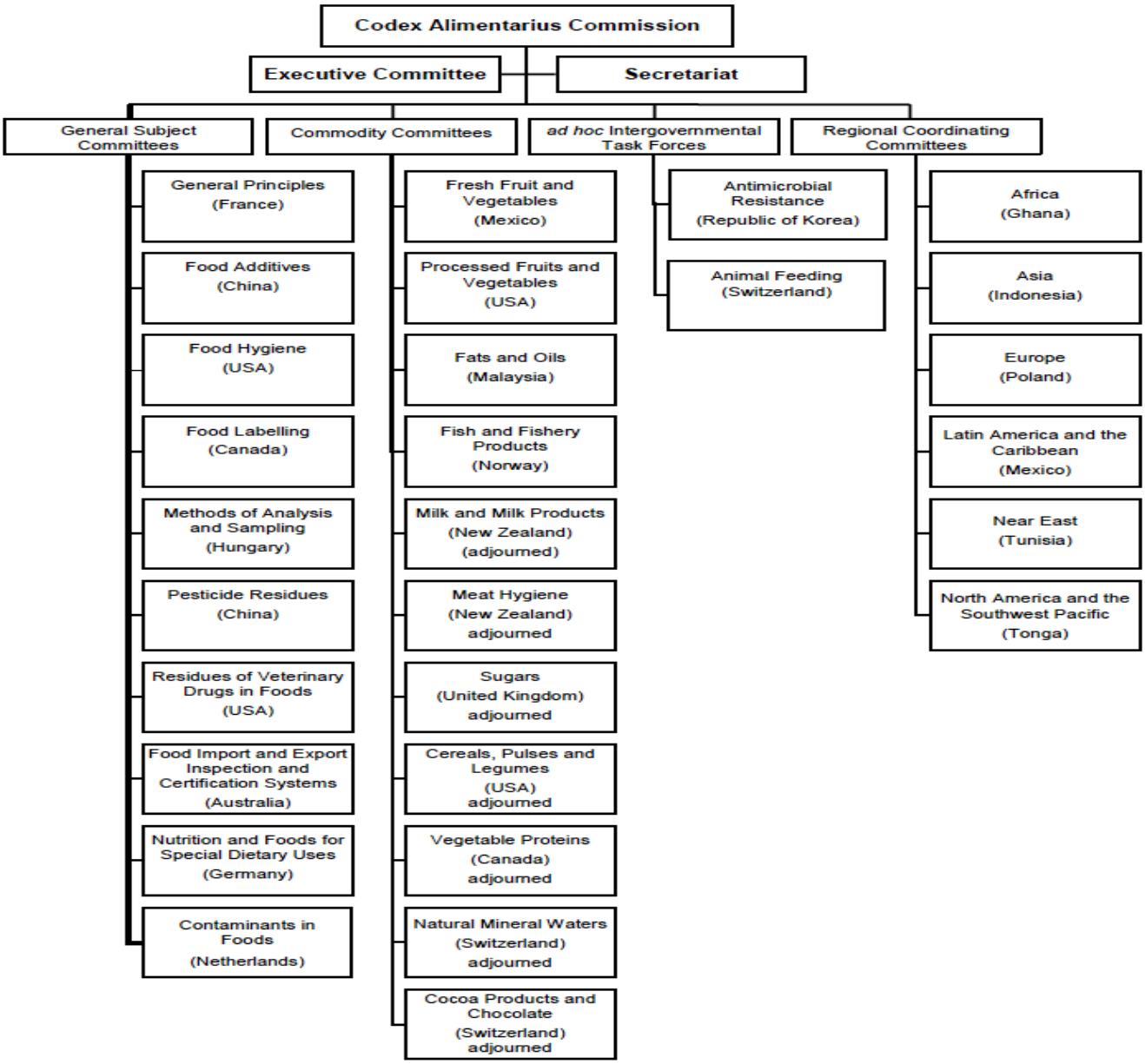


Figure 1 Joint FAO/WHO Food Standards Programme (FAO/WHO, 2011)

For food supplements, there are four related codex committees; The CCFL works over claim on the labelling of any food including food supplements, the CCGP considers a wide range of principles for food such as guideline on risk analysis, the CCFH provides guidelines on food hygiene and quality system of food production, whereas the CCNFSDU is a primary committee working for food supplements (Dumoff, 2004).

The major tasks of the CCNFSDU have been identified in terms of reference (Federal Ministry of Food) as follows:

1) To study specific nutritional problems assigned to it by the CAC and give advice to the Commission on general nutrition issues;

2) To draft general provisions, as appropriate, concerning the nutritional aspects of all foods;

3) To develop standards, guidelines or related texts for foods for special dietary uses, in cooperation with other committees where necessary; and

4) To consider, amend if necessary, and endorse provisions on nutritional aspects proposed for inclusion Codex standards, guidelines and related texts.

In 2012, the Federal Ministry of Food, Agriculture and Consumer Protection on behalf of the Federal Republic of Germany hosted the 34th CCNFSDU meeting held in Bad Soden am Taunus, Germany, on 3 to 7 December 2012 (Federal Ministry of Food).

One of the successful works completed by the CCNFSDU relevant to food supplements is "Guidelines for Vitamin and Mineral Food Supplements, CAC/GL 55-2005" (Codex, 2012b) fully adopted at the 28th CAC Session that was held in Rome on July 4-9, 2005 (U. S. FDA, 2012f). The guidelines apply only to supplements containing vitamins and/or minerals which are regulated as foods. Not only compositions of micronutrients, requirements of safety purity and bioavailability of the substances are addressed in the guidelines, but also the criteria on setting of minimal and maximum levels of each micronutrient are recommended. In addition, the guidelines clarify other safety requirements such as packing, labelling and claims (Codex, 2012b).

Codex Alimentarius including this food supplement guidelines are voluntary encouraged by the WTO to harmonise SPS measures among WTO members based on the WTO Agreement on the Application of Sanitary and Phytosanitary Measures or SPS Agreement (WTO, 2012)[8]. Moreover, they are used as a reference point for the resolution of trade dispute between the WTO members. However, under Article 3(3) of the SPS Agreement, the members may implement national SPS measures which are highly stricter than the codex standards if there is scientific evidence and it is necessary for protection of human, animal or plant life or health in their territories. In addition, the Codex Alimentarius are non-legally binding documents and the SPS agreement does not require members to adopt any codex document, unless a member adopts it as national regulation (Hathcock, 2005). Therefore, regulations and control measures of food supplements may differ in each country.

2.2 EU

In the EU, a principal food regulation is the Regulation (EC) No. 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirement of food law, establishing the EFSA and laying down procedures in matters of food safety[9] or called the "General Food Law Regulation (GFL)" which is applied to all foodstuffs including food supplements at all stages of food

[8] Article 3(1) of the SPS agreement
[9] Regulation (EC) No. 178/2002, OJ L 31,1.2.2002

chain. Under this regulation, common principles based on scientific approach, efficient organisational arrangement, procedure for decision-making in matters of food and feed safety, and responsibilities of relevant stakeholders with safe food production and distribution were established in order to protect public consumers at a high level as well as to support free-movement of foods among MSs (Coppens, Da Silva, et al., 2006).

Apart from the GFL addressing tasks and responsibilities of stakeholders related to foods, one of major directives related to food supplements, especially for vitamins and minerals is the Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the MSs relating to food supplements which was enacted and asked for all MSs to incorporate the EU Food Supplement Directive into national law by 31 July, 2003 with full compliance by July 2005 (Yeung et al., 2006). This directive not only establishes unique definition of food supplements, safety requirements, positive lists of permitted vitamins and minerals, and labelling criteria but also defines responsibilities of MSs, manufacturers, the EFSA, and the EC in order that food supplements marketed in EU are safely produced and controlled in a clear legal framework. Other related EU laws to food supplements such as the food labelling, presentation and advertisement (Directive 2000/13/EC), Nutrition and Health claims (Regulation 1924/2006), and Hygiene for food supplement production (Regulation 852/2004) also address responsibilities of relevant organisations (Krutmann et al., 2011).

Relevant organisations and their responsibilities with food supplements under these regulations and directives are summarised as follows:

2.2.1 EFSA

Basically, the EFSA is responsible for risk assessment, scientific advice, technical support and risk communication for European regulations in all issues regarding directly or indirectly to food and feed safety[10]. For food supplements, the EFSA has a task to evaluate the safety and bioavailability of nutrient sources proposed for addition of permitted substances in Annex II of the Directive 2002/46/EC. There were 39 out of 533 applications approved from the safety evaluation based on sufficient scientific knowledge and possible safety concern during 2005 – 2009. These evaluations were taken by the Panel of food additive and nutrient sources added to food (ANS panel) under the EFSA (EFSA, 2011). Moreover, the Scientific Committee on Food (SCF) and the Panel on dietetic products, nutrition and allergies (NDA) of EFSA were asked by the EC to determine the safe maximum and minimal levels of vitamins and minerals in food supplements (Eberhardie, 2007) to comply with Article 5 of the Directive of Food Supplements by performing a comprehensive evaluation of the possible adverse health effects of individual micronutrients at intakes exceeding the dietary requirements, and establishing Tolerable Upper Intake Levels (ULs) for various groups of consumers as possible (EFSA, 2011). The EFSA continuously reviews and re-evaluates safety aspects of vitamins and mineral based on available scientific information and publish opinions through the EFSA website. The EFSA also has to give advice and consultation to the EC for revision of the lists of vitamins and minerals in Annex I and II of the Directive[11] and the lists of ingredients in Annex IIIa of food labelling[12]. For the health claim, the EFSA has a major task to do pre-market approval of all health

[10] Article 22 of the Regulation (EC) No. 178/2002
[11] Article 14 of the Directive 2002/46/EC
[12] Article 6(11) of the Directive 2002/46/EC

claims based on risk assessment principle and scientific substantiation (Krutmann et al., 2011; Yeung et al., 2006).

2.2.2 EC

Under the GFL, the EC takes responsibilities on risk management and risk communication on food safety[13]. The EC cooperating with MSs and the EFSA to achieve the general objective of a high level of human health protection based on risk analysis[14] by considering risk assessments and relevant regulatory factors, weighting political and social alternatives and selecting appropriate safety requirements for food placed in the regional level. Moreover, The EC by collaborating with EFSA and MSs through the RASFF network[15] takes actions on communication, management and adoption of implementing measures when an incident, emergency or crisis situation rises[16].

For food supplements, all risk management and decision-making process are responsible by EC assisting with the Standing Committee on the Food Chain and Animal Health[17], which consists of experts from MSs (Coppens, Da Silva, et al., 2006). After The EFSA has published the scientific report on ULs for vitamins and minerals since 2006, the EC is on the process of defining maximum levels and selecting the risk management model for determining the maximum amounts of vitamins and minerals for addition to regular food. A discussion paper on the setting of maximum and minimum vitamins and minerals in foodstuffs (EC, 2006) is now available and circulated to both MSs and relevant stakeholders for their response before further discussion. However, the final decision on establishment of maximum and minimum amounts of vitamins and minerals in foodstuffs and food supplement is not yet achieved (EC, 2007a). Furthermore, the EC has considered additional substances in the positive lists of the Directive 2002/46/EC which therefore has been amended by the Commission Directive 2006/37/EC of 30 March 2006, the Commission Regulation (EC) No 1170/2009 of 30 November 2009, and the Commission Regulation (EC) No 1161/2011 of 14 November 2011 (EC, 2012c).

2.2.3 FVO

The FVO plays an important role in food safety control in EU by supporting inspection in MSs and Third countries, audit, and verification of food safety control programme. Responsibilities of the FVO, especially for food safety are as follows (EC, 2012a):

1) Check on compliance with the requirements of EU food safety and quality legislation within the EU on compliance with EU import requirements in the third countries exporting to the EU. The FVO contributes inspectors to audit the third countries which would like to export food products to place in the EU market.

2) Develop and implement effective control system in the food safety sector by developing annual inspection programme, identifying priority areas as well as countries for inspection. By this task, the inspection programme in EU is kept up-to-date and published through the EC website.

[13] Article 3(12)- 3(13) of the Regulation (EC) No. 178/2002
[14] Article 6 of the Regulation (EC) No. 178/2002
[15] Article 50-52 of the Regulation (EC) No. 178/2002
[16] Article 53-56 of the Regulation (EC) No. 178/2002
[17] Article 13 of the Directive 2002/46/EC

3) Develop EU policy in food safety especially in monitoring and inspection areas.

According to the FVO works on development and evaluation of the inspection programme in MSs and third countries including recommendations for strengthening inspection programmes, the post-market control system would be assured that consumer protection is highly achieved in all MSs and complied with relevant food legislations. However, an inspection programme especially for food supplements is mainly developed by MSs and may be recommended and/or evaluated by the FVO according to their roles.

2.2.4 MSs

MSs have main responsibilities to enforce food law including relevant food regulations and monitor implementation of FBOs at all stages of the food supply chain at the national level[18]. An official control system, specific rules or measures can be appropriately implemented based on the risk analysis principle and a high level of consumer protection without barriers to trade with other MSs. The MSs also shall participate in the risk communication with EC, EFSA and FBOs in order that any unsafe food situation can be timely controlled and preventive measures adopted by EC are effectively implemented[19].

For food supplements, MSs were required to firstly bring the directive 2002/46/EC into force the national law[20]. Furthermore, monitoring system of food supplements, their production, labelling and presentation including additional activities should be provided based on relevant directives and regulations to ensure that these products are placed on the internal market only if they comply with the rules of this directive and national requirements[21]. In cases of new information or reassessment of food supplements resulting in questions of safety for consumption, the MSs have tasks to temporarily suspend and immediately communicate to the EC for further discussion and adoption of appropriate measures[22].

Apart from the Directive of Food Supplement, the MSs also can specifically regulate national requirements or regulations to control food supplements based on domestic consumption data, scientific evidences and necessity for consumer protection without trade barrier in the regional market. For example, competent authorities of some MSs may require pre-market authorisation for new food supplement products which contain ingredients other than in the positive lists of the Directive. The procedures and requirements may differ from each MS (Krutmann et al., 2011). Another example is about health claims for food supplements, most of MSs have informal pre-approval systems while the post-market claim approval is normally handled by different post-clearance systems (Yeung et al., 2006).

2.2.5 FBOs

FBO(s)[23] is comprehensively defined from producing to catering foods including food supplements for consumers shall ensure that their products produced and marketed in EU are complied with relevant safety requirements[24], and in case of non-compliance, corrective measures shall be immediately taken such as

[18] Article 17(2) of the Regulation (EC) No. 178/2002
[19] Article 50, 53-54 of the Regulation (EC) No. 178/2002
[20] Article 15 of the Directive 2002/46/EC
[21] Article 3 of the Directive 2002/46/EC
[22] Article 12 of the Directive 2002/46/EC
[23] Article 3(6) of the Regulation (EC) No. 178/2002
[24] Article 17 of the Regulation (EC) No. 178/2002

product withdrawal from the market and/or recall from the consumers as well as communicating to competent authority for more effective elimination of the risk[25]. Moreover, FBOs have to establish the traceability system for timely tracing, tracking, and controlling any potential risk in the food production chain[26]. With any damage of consumers caused by defective food products, the FBOs shall be liable and take a responsibility according to the Directive 85/374- liability for defective products[27].

For Food supplements, more specific regulations shall be complied based on the Directive 2002/46/EC, relevant regulations as well as national requirements as applicable. FBOs shall produce food supplements containing permitted ingredients set in the positive list. The quality, purity, consistency and stability of the products shall be controlled through compliance with GMP for foodstuffs (Hanekamp & Bast, 2007). FBOs have to provide label and claims of food supplements that comply with the related requirements and shall inform the competent authority when placing in the market in order to not only support efficient monitoring system but also avoid misleading to consumers and confusing with other products such as herbal remedies, medicinal products.

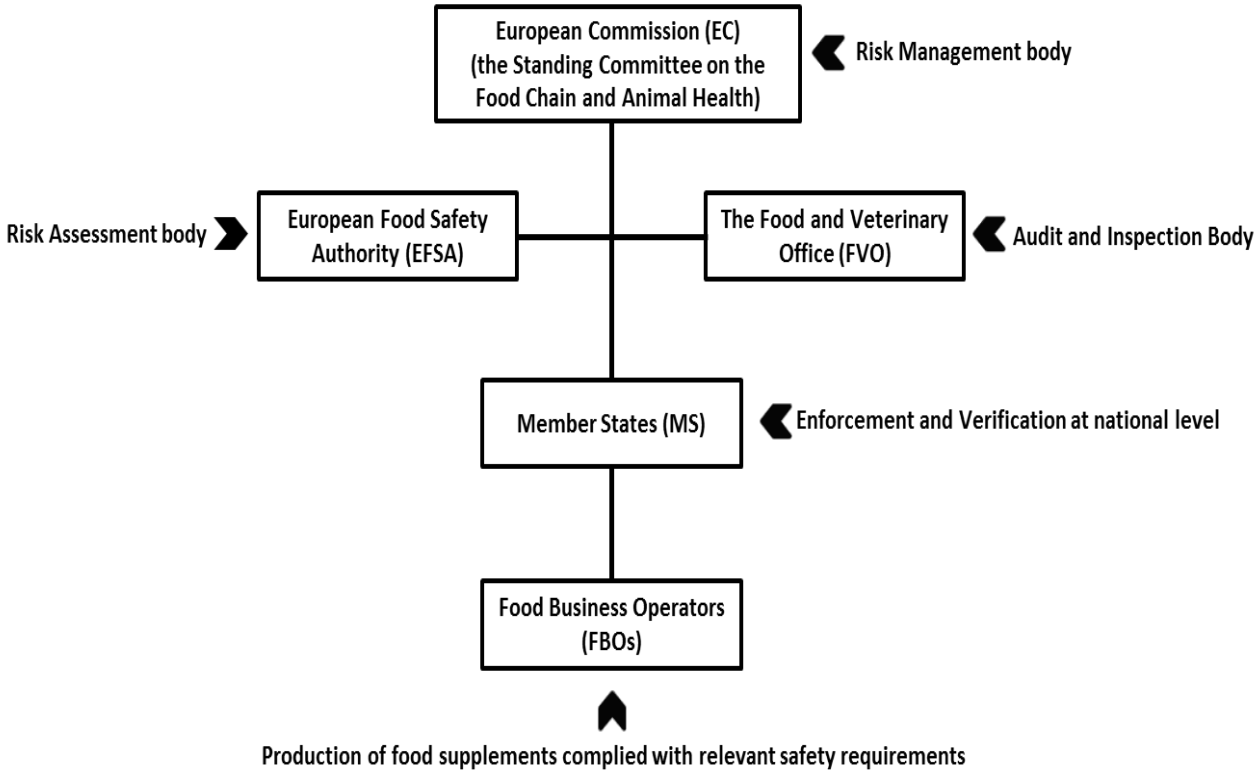


Figure 2 Relevant organisations related to food supplements in EU.

[25] Article 19 of the Regulation (EC) No. 178/2002
[26] Article 18 of the Regulation (EC) No. 178/2002
[27] The Council Directive 85/374/EEC of 25 July 1985 on the approximation of the laws, regulations and administrative provisions of the Member States concerning liability for defective products.

2.3 US

The Dietary Supplement and Health Education Act (DSHEA) of 1994 (U. S. FDA, 1994) signed into law on October 25, 1994 is a major regulation to control dietary supplements from production based on current GMP (CGMPs), labelling requirements and claims (Wollschlaeger, 2003). This regulation defines definition of dietary supplements separately from drugs (Hanekamp & Bast, 2007; S. A. Mason, 2010). It is also an industry-friendly legislation since the U.S Congress considered and passed this Act based on a main reason that "dietary supplements are safe within a broad range of intake, and safety problem with the supplements are relative rare" (S. A. Mason, 2010)[28] . From this regulation, two additional governmental bodies were established, namely the Commission on Dietary Supplement Labels[29] and the ODS[30]. The DSHEA amends the Federal Food, Drug, and Cosmetic Act (FD&C Act) of 1938 to include the regulation and labelling systems on dietary supplements (Wollschlaeger, 2003) while roles of the U.S. FDA are changed for this product.

Moreover, other regulations related to dietary supplements in US are the Nutrition Labelling and Education Act (NLEA) of 1990 requiring scientific evaluation and approval standard for health claims whereas the Food and Drug Administration Modernization Act of 1997 containing an expanded procedure for authorisation health claim for food. The Dietary Supplement and Nonprescription Drug Consumer Protection Act of 2006 (U. S. FDA, 2006a) mandates manufacturers, packers or distributors of dietary supplements to submit all serious adverse event reports to the HHS.

Relevant stakeholders and their responsibilities on safety of dietary supplements focusing on vitamins and minerals are summarised as below:

2.3.1 The Commission on Dietary Supplement Labels

An independent agency within the executive branch[31] composes of 7 members appointed by the President with expertise requirements[32]. The seven members of commission appointed by the president in October, 1995 consist of three nutritionists, two experts on herbs, one attorney, and a specialist in government relations and public affairs ("DSHEA Summary & Analysis,"). Functions of this commission[33] are to conduct a study on dietary supplement label claims and provide recommendations for the regulation of label claims and statements for these relevant products. The best truthful, scientifically valid and appropriate information should be evaluated in order to avoid consumers from confusing or misleading information. After a final report is submitted to the President and the Congress within 24 months, the Secretary of HHS must implement any necessary regulatory changes, through formal regulations within two years[34].

[28] Mason, 2010, p. 112
[29] Section 12 of the DSHEA of 1994
[30] Section 13 of the DSHEA of 1994
[31] Section 12 (a) of the DSHEA of 1994
[32] Section 12 (b) of the DSHEA of 1994
[33] Section 12 (c) of the DSHEA of 1994
[34] Section 12 (e) of the DSHEA of 1994

2.3.2 HHS

Missions of HHS are to protect all Americans 'health and provide essential human services, especially for people who are least able to help themselves. The HHS works closely with state and local governmental bodies on health programmes for justifiable treatment of beneficiaries countrywide (HHS). Besides, ten regional offices hosted by the Office of Intergovernmental and External Affairs work closely with state, local, and tribal levels in order to ensure that all relevant responsibilities of HHS are successfully achieved. Each regional office is managed by a Regional Director who is appointed by the U.S. president (HHS).

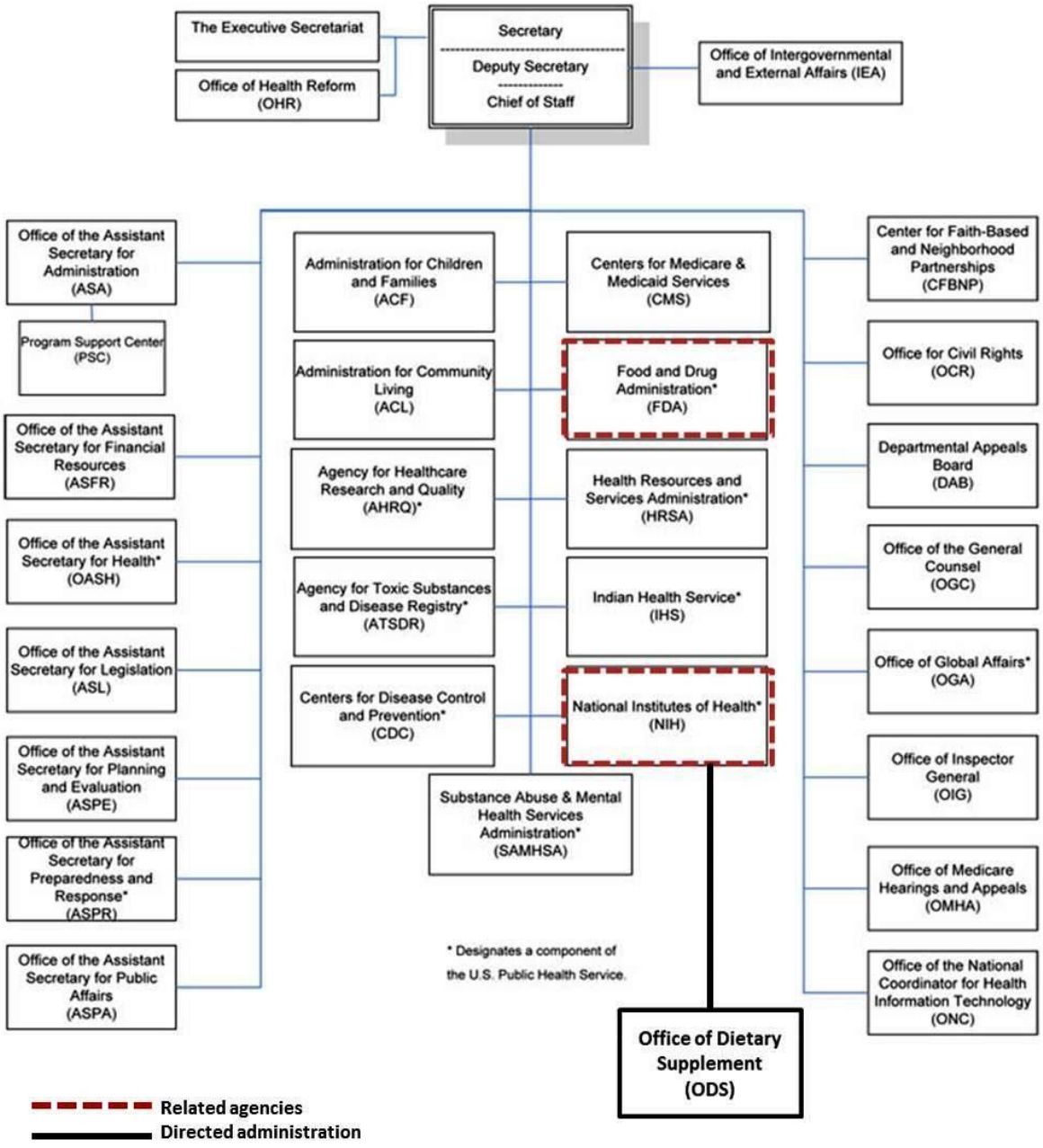


Figure 3 HHS Organisational Chart (modified from HHS website (HHS))

There are two main agencies straight related to dietary supplements:

2.3.2.1 ODS

The ODS is mandatory established in 1995 within the National Institutes of Health (NIH) under the HHS[35] in order to strengthen knowledge and understanding of dietary supplements by promoting scientific research in the area of dietary supplements. Responsibilities of ODS[36]are described (ODS) as follows;

1) Explore more fully the potential role of dietary supplements as a significant part of the efforts of the United States to improve health care.

2) Promote scientific study of the benefits of dietary supplements in maintaining health and preventing chronic disease and other health-related conditions.

3) Conduct and coordinate scientific research within NIH relating to dietary supplements.

4) Collect and compile the results of scientific research relating to dietary supplements, including scientific data from foreign sources.

5) Serve as the principal advisor to the Secretary and to the Assistant Secretary for Health and provide advices to the Director of NIH, the Director of the Centres for Disease Control and Prevention, and the Commissioner of the Food and Drug Administration on issues relating to dietary supplements.

Duties of the ODS result in significant improving human health and preventing chronic disease and other health related condition based on the scientific sounds (Wollschlaeger, 2003).

2.3.2.2 U.S. FDA

The U.S. FDA established within the HHS has primary responsibilities on dietary supplement in aspects of

1) Providing proven evidence if the dietary supplement is adulterated[37]. In such a case, the HHS is mainly responsible to order the product withdrawal.

2) Giving pre-market authorisation in case of new ingredients of dietary supplements only[38] .

3) Requiring manufacturers to notify statements of nutritional support within the period[39].

4) Establishing of CGMPs for dietary supplements[40] that results in requiring expiration date labelling on dietary supplements.

5) Monitoring supplements after they are placed on the market, especially in claims on the product labelling including packages based on the FD&C Act. For an example, stop any company from selling an unsanitary or some toxic dietary supplements (Wollschlaeger, 2003).

[35] Section 13 (a) of the DSHEA of 1994
[36] Section 13 (c) of the DSHEA of 1994
[37] Section 4 of the DSHEA of 1994
[38] Section 8 of the DSHEA of 1994
[39] Section 6(6) of the DSHEA of 1994
[40] Section 9 of the DSHEA of 1994

2.3.3 FTC

The Bureau of Consumer protection of FTC has main responsibilities on consumer protection against unfair, deceptive, or fraudulent practices in the marketplace based on the FTC Act of 1914. Investigation and complaints from consumers are conducted by the Bureau to take any measure for consumer protection. Moreover, development of relevant rules and consumer education are also mainly tasks of this agency (FTC, 2012).

For dietary supplements, the FTC cooperating with U.S. FDA under the FTC-FDA Liaison Agreement has primary responsibilities for claims for advertising, including print and broadcast advertisement, infomercials, catalogues, website and other direct market materials. Deceptive advertisements are broadly not permitted[41], while false advertisements of drugs, devices, services, cosmetic, and food including dietary supplements are prohibited[42]. "Dietary Supplements: An Advertising Guide for the Industry" (FTC, 2001) has been published to facilitate business who produce and advertise dietary supplements in the U.S. market.

2.3.4 Agencies at the state level

In principle, the federal law is the supreme law of the nation. However, an exclusive state regulation can be enacted if there is perceived by the U.S. congress based on necessary for health and safety with commercial balance (Law, 2005)[43]. Moreover, competent authorities working on the food safety control and enforcement areas may differ depending on each state, for examples, in New York City, the Department of Health (DOH) and the Department of Agriculture & Markets (DAM) are main agencies collaborating on food regulations and enforcement including dietary supplements whereas the Department of State Health Service in Texas has a major task to control food product and dietary supplements as well as consumer education (Texas, 2011). For dietary supplements, several states implement no regulation beyond that required by federal law like the DSHEA while some states apply additional actions than the federal requirements such as warning label, retail restriction measures (Law, 2005).

2.3.5 FBOs

Since the U.S. FDA shall bear the burden of proof on safety issues of dietary supplements, manufactures are not required to demonstrate effectiveness of dietary supplements before placing on the market, unless there are new ingredients and/or health benefits are claimed as defined under the DSHEA (Hatchcock, 2001). However, the manufacturers shall take responsibility on ensuring quality assurance, product safety, product efficacy, the accuracy of product claims and the application of food standard CGMPs. To comply with these responsibilities, the manufacturers have to provide (Brownie, 2005):

1) Quality assurance data assuring that the product are safe and complied with requirements,

2) Evidences that substantiates product claims,

3) Information and record data about product registration, however, they are not required by law to register their products with the U.S. FDA, and

[41] Section 5 of the FTC Act of 1914
[42] Section 12 and 15 of the FTC Act of 1914
[43] New York State Task Force on Life & the Law, 2005, p.69

4) Evidence of compliance with food standard CGMPs.

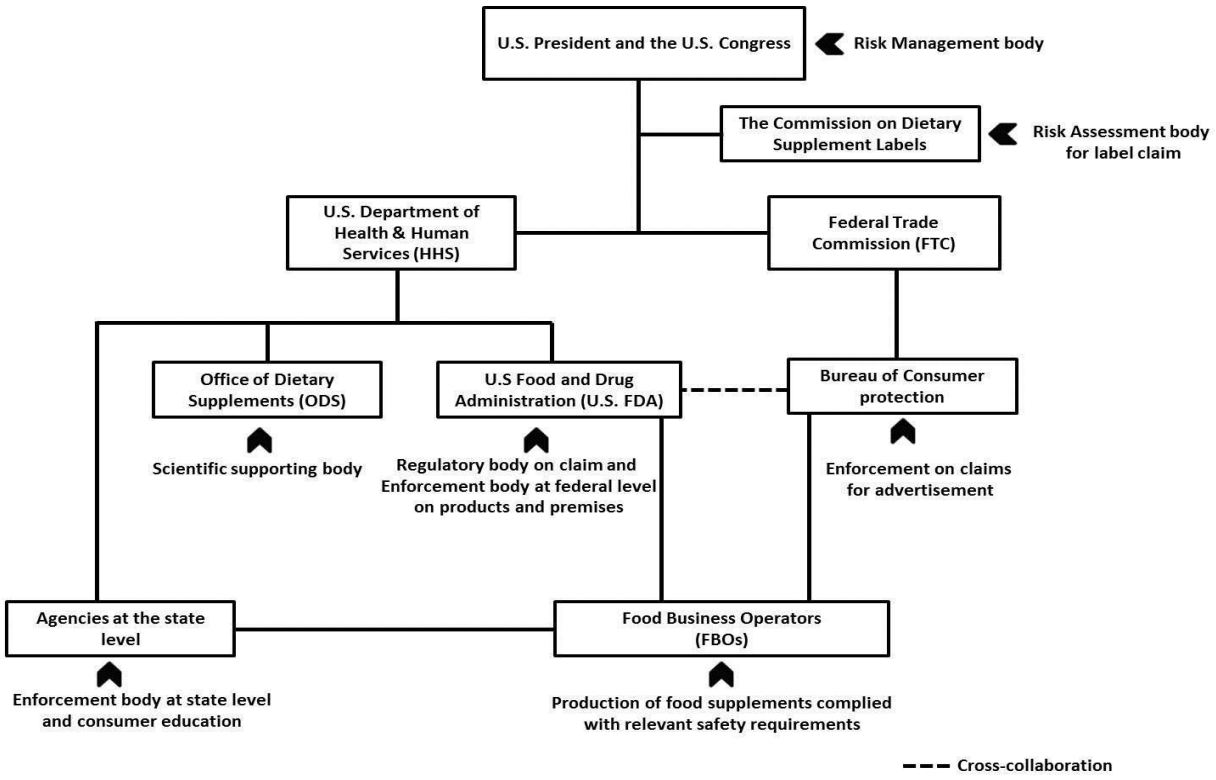


Figure 4 Relevant organisations related to dietary supplements in US.

2.4 Thailand

The fundamental law to control food safety in Thailand is the Food Act B.E. 2522 (1979) (T. FDA, 1979) giving a clear definition of food including relevant key words[44], assigning the MoPH to be in charge of the execution of this Act to appoint competent officers, legislating Ministerial Regulations, Notifications of MoPH, Announcements of the Food and Drug Administration and setting up other activities in order to reach mission of this Act[45]. It also determines comprehensive scopes of controlling quality and safety in foods such as methods of production, importation, ingredients used in foods, containers and packages, labels, inspection and seizure, and method of analysis[46]. The Food Commission and assigned tasks are addressed under chapter 1 of the Act.

Apart from the Food Act, a notification of the MoPH (No. 293) B.E. 2548 (2005) (T. FDA, 2005) mainly applies to both domestic and imported dietary supplements as defined in clause 2 and 3 of the notification. A positive list of permitted substances shall be issued by the Thai FDA and approved by the Food Commission before compulsory implementation in the national level[47]. Moreover, safety requirements on

[44] Section 4 of the Food Act B.E. 2522 (1979)
[45] Section 5 of the Food Act B.E. 2522 (1979)
[46] Section 6 of the Food Act B.E. 2522 (1979)
[47] Clause 4(1) and 4(5) of the notification MoPH (No. 293) B.E. 2548 (2005)

ingredients, contamination, production, labelling, health claim, and packaging have been described under this notification by referring to relevant regulations such as notifications of the MoPH for Food additives, GMP, Packaging, Labelling, and Health claims.

Under these regulations, many competent agencies are involved with different responsibilities on safety and quality control for dietary supplements which can be described as follows.

2.4.1 Food Commission

The Food Commission is established under section 7 of the Food Act B.E. 2522 (1979) which consists of the Permanent Secretary of the MoPH acting as Chairman, Secretary General of the Thai FDA, Director General of the Health Department or representative, Director General of Medical Service Department or representative, Director General of the Communicable Disease Control Department or representative, Director General of the Medical Science Department or representative or representative, Director General of Science and Service Department or representative, Director General of Department of Domestic Trade or representative, Director General of Customs Department or representative and representatives from the Ministry of Defense, Ministry of Agriculture and Legislative Commission. Under this section, the Deputy Secretary-General of the Thai FDA is appointed to be secretary of the commission while the director of Bureau of food acting as secretary assistant. Moreover, The Minister in charge of chairman shall appoint not more than 9 qualified persons as members of the food commission. Among 9 persons, representatives of FBOs shall not more than 4 persons. The members of food commission appointed by the Minister shall have a team of two years and may be reappointed[48]. By considering the members of the food commission, all relevant stakeholders covering food chain are involved.

Responsibilities of the food commission[49] are

1) Promulgation of regulations in order to control quality and safety of food[50]

2) Consideration on application for extension of licence and the granting of licence to produce food for sale in Thailand[51].

3) Withdrawal of the product licence[52].

4) Decision making on any action to destroy or treat food or containers in any way as appropriate if there is evidence showed that it is either impure, adulterated, substandard, specified by the Minister, or hazardous to public health which is not complied with relevant food regulations[53].

5) Consideration on suspension or revoke of the licence if there is evidence showed that the produced food is not complied with relevant regulations[54].

[48] Section 9 of the Food Act B.E. 2522 (1979)
[49] Section 8 of the Food Act B.E. 2522 (1979)
[50] Section 6 of the Food Act B.E. 2522 (1979)
[51] Section 19 of the Food Act B.E. 2522 (1979)
[52] Section 39 of the Food Act B.E. 2522 (1979)
[53] Section 26-29 of the Food Act B.E. 2522 (1979)
[54] Section 46 of the Food Act B.E. 2522 (1979)

2.4.2 MoPH

The MoPH is a principle agency in Thailand responsible on public health at the national level. Minister of the MoPH assigned by the Prime Minister takes managerial tasks to successfully accomplish the missions (Health, 2008) which are

1) Determination of national and international health policy and strategy in accordance with current situation.

2) Development of effectively integrated health service system in order to facilitate public health in both general and emergency circumstances.

3) Support the society to improve potential health and behaviours.

4) Development of health management system based on adequate standard and sustainable mechanism.

5) Determination of health research areas and knowledge management

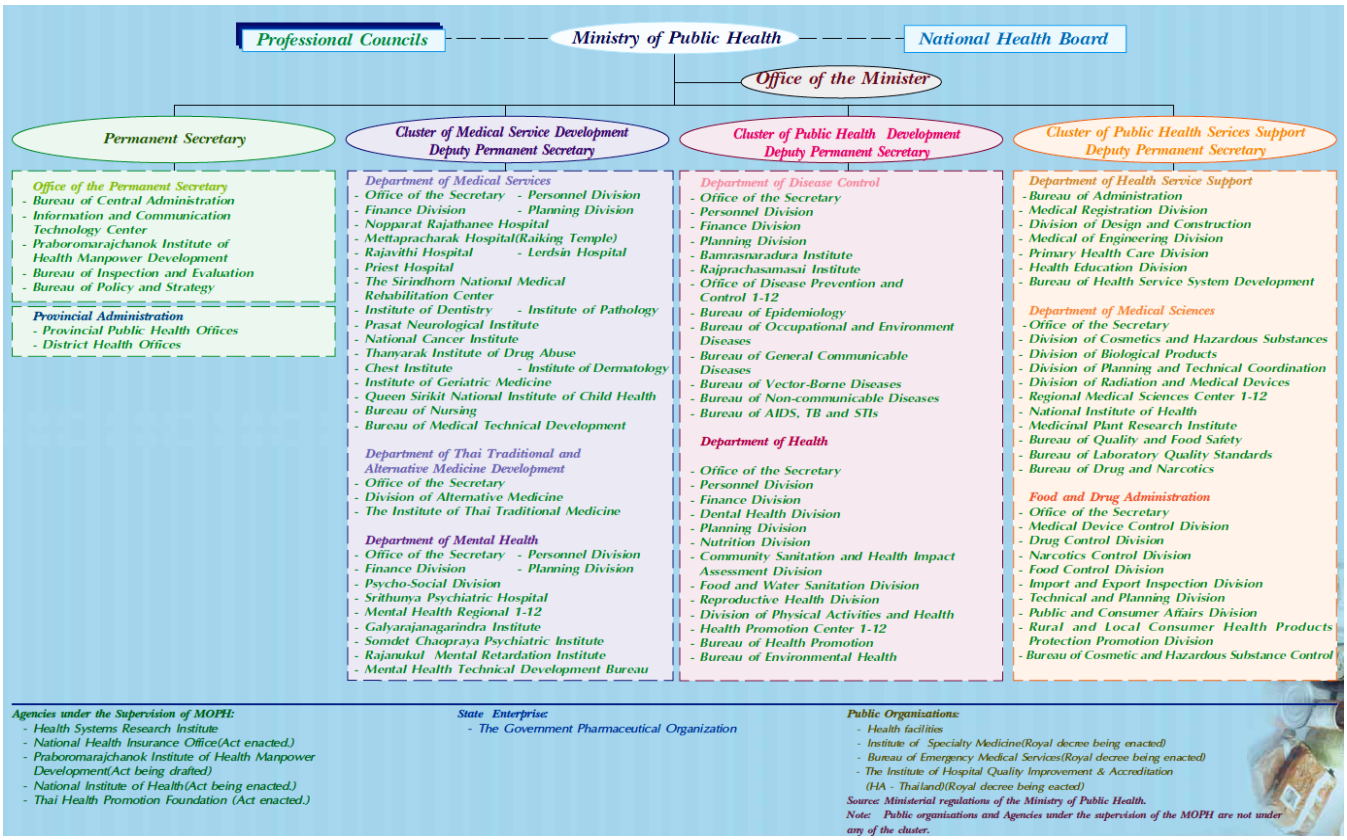


Figure 5 Organisation structure of the MoPH of Thailand (T. FDA, 2004a)[55]

A main responsibility on risk assessment and advisory options to the Food Commission for further decision making is taken by sub-committees which were established and revised by the Food Commission in

[55] Thai FDA, 2004, p.6

August 31st, 2012[56]. Each sub-committee composes of experts specifically in scientific skill and knowledge related to risk assessment, representatives from governmental agencies relevant with nutrition, analytical methods, agricultural commodities, animals, and foods, representatives from academic institutes like Institute of Nutrition, representatives from public and consumer sectors like the Office of Consumer Protection Boards, Foundation of Consumer as well as from private sectors such as the federation of Thai industries.

For risk assessment of dietary supplements focusing on vitamins and minerals, there are 7 sub-committees working for specific related aspects, namely sub-committee on Problem analysis and Technical researches, sub-committee on Nutrition and Nutrition & Health Claims, sub-committee on Food Additives, sub-committee on Packaging, sub-committee on Analytical Methods for Food, sub-committee on GMP & Food Production Facilities, and sub-committee on Food Labelling. These sub-committees discuss and analyse scientific information and researches from both national and international data to assess the potential risks related to supplements before providing options and advices to the Food Commission, as well as developing guidelines and/or criteria for manufacturers, consumers and officers in order to implement the food regulation effectively. In some cases, working groups are temporary established under the Bureau of Food to support the relevant sub-committees by collecting scientific data and studying regulations or measures of supplements in other countries.

Apart from sub-committees and working groups, several competent authorities under the MoPH are also responsible for working to control safety and quality of products before and after placing on the market in order to protect consumer health. They are as follows:

2.4.2.1 THAI FDA

The Thai FDA established under the cluster of Public Health Service Support of the MoPH plays a main role to protect consumer health, especially to ensure safety, quality and efficacy of health products that includes foods, drugs, psychotropic substances, narcotics, medical devices, volatile substances, cosmetics and hazardous substances sold in the territory. The regulations, enforcement, preventive measures and other activities related to consumer protection are implemented in accordance with national legislations and international agreements (T. FDA, 2004c). The Thai FDA takes responsibilities in five main areas:

1. Pre-market control that includes manufacturing facilities, product quality, safety, and advertisement before placing in the market.

2. Post-market control such as investigation of product and premises to ensure that they maintain compliance with relevant regulations and requirements. A sampling plan is a tool used for both domestic and imported products to achieve these compliances.

3. Surveillance programme including research and epidemiological data on adverse effects and information exchange to detect unexpected outcomes from consumer resulting from usage of products controlled under Thai FDA.

4. Consumer education through public media such as television, radio, newspaper, leaflets, internet, as well as active campaigns conducted in department stores, schools and villages in order to support accurate and useful information to consumers.

[56] Section 12 of the Food Act B.E. 2522 (1979)

5. Technical Support and Cooperation with other agencies in food supply chain.

Under the Thai FDA, three main agencies work specifically related to dietary supplements;

1) Bureau of Food

The Bureau of Food has been promoted from the Food Control Division since 2011 to take main responsibilities for food control on quality and safety under the Food Act B.E. 2522 (1979) which are summarised as follows:

1. Setting up food standards and specifications as well as hygienic and labelling requirements;

2. Controlling the domestic production and importation of food products;

3. Reviewing/granting approvals for the registrations of foods as defined in regulations including advertisements and packaging materials;

4. Inspecting food manufacturing premises and sellers;

5. Conducting sampling and quality assessments of food products as well as epidemiological studies;

6. Taking legal actions, e.g. seizure, product recalls, prosecution;

7. Promoting consumer awareness and voluntary compliance of food manufacturers;

8. Controlling food-producing plants so that they meet national standards by using GMP;

9. Collaborating with other government agencies, the private sector as well as international organisations in the matters related to Technical Corporation and information exchange

2) Rural and Local Consumer Health Products Protection Promotion Division (RLCP)

The RLCP division established in 2002 mainly works as the cooperating centre between the Thai FDA and 77 Provincial Public Health Offices across Thailand in order to promote, support, and develop health product quality and safety in the rural and local areas. The RLCP also facilitates information related with regulations and implementing measures approved by The Thai FDA to all Provincial Public Health Offices as well as other governmental agencies related to food in normal and emergency situations (T. FDA, 2004b).

3) Bureau of Import and Export Inspection

The Bureau of Import and Export Inspection is in charge of inspection and monitoring imported health products including foods[57] at 35 checkpoints (T. FDA, 2011b) crossing all borderlines in Thailand by effectively collaborating with other agencies under the Thai FDA and other departments under the MoPH. Moreover, other ministries relevant with a food chain such as the Customs Department, the Ministry of commerce, the Ministry of Industry, the Ministry of Agriculture and Agricultural Cooperatives collaborate with this agency to develop monitoring and surveillance plan as well as relevant activities for the law compliance and consumer protection.

[57] Section 15-16 of the Food Act B.E.2522 (1979)

2.4.2.2 PROVINCIAL PUBLIC HEALTH OFFICES

All 77 Provincial Public Health Offices play an important role on monitoring, enforcing and taking any actions approved by the Thai FDA based on the Food Act B.E. 2522 (1979) and relevant food regulations. These offices also support controlling food safety at the provincial and local levels by developing food sampling plans in accordance with the annual sampling plan of the Thai FDA. In case of emergency situation, the Provincial Public Health Offices collaborate with relevant authorities to take any action in that responsible area to timely protect consumer health as well as to educate consumer on food safety.

2.4.2.3 DEPARTMENT OF MEDICAL SCIENCE (DMSc.)

The DMSc. serves as the national reference laboratory in Thailand and provides analytical services for medical, cosmetic, medical device, herbal and health products based on relevant regulations. This agency also supports development of laboratory units in regional levels which recently are 14 Regional Medical Science Centres in order to support roles of DMSc. at regional, provincial and local areas (DMSc., 2011). For food products including dietary supplements, the Bureau of Quality and Safety of Food (BQSF) under the DMSc. is in charge of a national reference laboratory for food and analytical method development. Responsibilities of the BQSF are as follows (BQSF):

1. Providing services for food analysis to protect consumers and improve the quality of food production.

2. Conducting and developing research on analytical methods for routine use.

3. Conducting quality assurance activities to assure the quality of analytical performance.

4. Cooperating and coordinating with national and international organisations in areas of food and food-related.

5. Developing food test kits for use outside laboratory and conducting food safety programme to support the national food safety policy.

Dietary supplements both launched in the market and imported into Thailand shall be sampled by the Thai FDA and analysed by the BQSF based on the related regulations. Results of the analysis are mainly considered by the Thai FDA for law enforcement.

2.4.3 FBOs

According to the Food Act B.E. 2522 (1979) and relevant regulations on dietary supplements, FBOs shall produce or import and control the food products both before- and after- placed on the domestic market. Scientific evidences and results of analytical testing shall be provided and submitted through the pre-market authorisation. In addition, facilities of the production, labelling, packaging, health claims, and advertisement shall be complied with the regulations addressed in the Notification of MoPH Re: Dietary Supplements. The FBOs also closely collaborate with competent authorities in case of any action taken to protect consumer health. The FBOs shall be punished[58], if the supplement is not complied with mandatory requirements.

[58] Chapter 8 of the Food Act B.E. 2522 (1979)

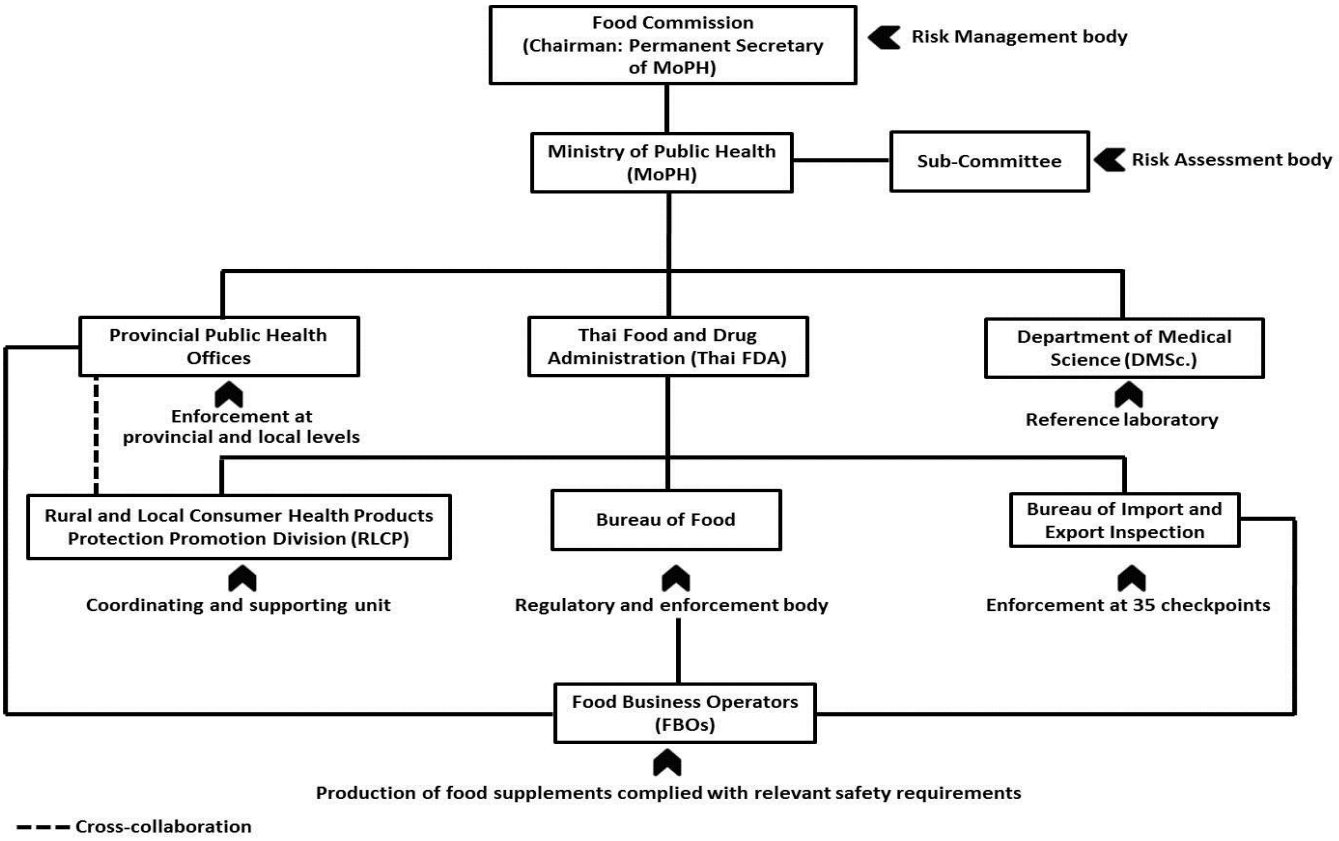


Figure 6 Relevant organisations related to dietary supplements in Thailand.

2.5 Summary

In a short summary, food supplements are significantly controlled by both international and national organisations. The CAC plays an important role of risk management at international level collaborating with many Codex committees responsible on risk assessment to provide guidelines and recommendations regarding the supplements. According to the WTO and SPS agreements, the WTO members including EU, US, and Thailand actively participate in the CAC and relevant Codex meetings for developing these codex guidelines based on the main purposes that are consumer protection and fair trade facilitation. At regional and national levels, EU, US, and Thailand have assigned several agencies to legislate and monitor micronutrient supplements sold on the market on the basis of risk analysis principle in order to protect consumer health, control reliable information for consumer choice, and facilitate trade in both domestic and international markets. In EU, the EC is in charge of risk management at the regional level, whereas all MSs take responsibilities on legal enforcement and monitoring product compliance. Comparing to US and Thailand systems, the EU has more potential risk assessment since the EFSA is an independent agency supporting technical and scientific options to the EC and MSs without trade interferes. The U.S. FDA and the FTC are mainly agencies for controlling food supplements in US, while the Thai FDA is one major agency to handle a lot of work on food supplements that may affect the effectiveness of consumer protection. Regarding the study on organisation aspect, there are many stakeholders involved in each regulatory system of food supplements; therefore, defined responsibility, clear collaboration and active communication are essential elements of the efficient control system.

3. REGULATIONS AND PRE-MARKET CONTROL SYSTEMS

With regard to the second chapter, various agencies are involved in the regulatory system of food supplements. Different countries have diverse management systems and legislations to ensure that these products are safe for consumption and make consumers more confident on the level of protection. This chapter would like to elucidate regulations on food supplements compulsory applied in EU, US, and Thailand based on perspectives of products that include substances, proper levels of micronutrients; premises with its facilities; and presentations that cover labels, claims, and advertisements. Furthermore, the obligations on pre-market authorisation addressed under the laws in EU, US, and Thailand will be described to understand the mechanism of this process and impact on the consumer protection. More specific requirements at national level as Ireland and New York case studies will be accessed in this chapter to learn about the linkage with regional or federal level, practical measures for enforcement, as well as to suitably compare with the regulatory system in Thailand.

Since one of the main problems regarding food supplements relates to consumer confusion between the supplements and other products like medicine, novel foods, GM products, and fortified foods, definitions and borderlines between the supplements and these similar products are clarified in this chapter with some examples giving for more understanding.

3.1 The definition of food supplements

In many cases, consumers may not distinguish food supplements from other foods resulting in misuse, while FBOs may not clearly classify food supplements to consumers and competent authorities that lead to non-compliance with relevant regulations. Hence, a clear definition of food supplements addressed in the food laws is essential to obviously explain scope of food supplements, active ingredients, and characterisation of the products that help to avoid problem of confusion.

3.1.1 Definitions of food supplements in EU, US, and Thailand

Food supplements or Dietary supplements have been clearly defined in relevant national regulations. Under the Article 2 of EC directive 2002/46/EC, Food Supplements are “foodstuffs the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form, namely forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids and powder designed to be taken in measured small unit quantities”. The nutrients under this directive are solely vitamins and minerals, however, other substances such as botanical, phytonutrients, enzymes, and essential fatty acids are often restricted by each MS based on national regulations and a principle of “mutual recognition” (Schwitters et al., 2007). In US, the dietary supplements defined in Section 3 of the DSHEA are “any product (other than tobacco and conventional food) intended to supplement the diet that bears or contains one or more of the following ingredients a vitamin, a mineral, herb or other botanical, an amino acid, a dietary substance for use by man to supplement to total dietary intake, or a concentrate, metabolite, constituent, extract, or combination of any ingredient described in the previous list”. However, these ingredients may not be regulated as food additives and may not include unproved new drugs, antibiotics, or biological substances. By this definition, three groups of dietary supplements based on function or origin are clarified (Hatchcock, 2001): 1) substances with nutritional properties such as vitamins, minerals, amino acids and fatty acids; 2) botanical

products providing various functions on physiologic roles; and 3) other substances such as steroid hormone precursors, pyruvate, and chondroitin sulphate. In Thailand, dietary supplements mean[59] "products taken for consumption other than conventional foods which contain nutrients or other substances as ingredients, are in forms of tablets, capsules, powders, flakes, liquids or others; which are not conventional food for consumers who expect for benefit of health promotion". Nutrients or other substances[60] cover vitamins, amino acids, fatty acids, and minerals, produces obtained from plants or animals including concentrates, metabolites composition or extracts of substances, alone or in combinations. Moreover, other substances which are not yet listed under this notification can be included after approval by the Food Committee. By these definitions, key characterisations can be summarised and compared as below table:

Table 1 Comparison on definitions of food supplements from EU, US, and Thailand laws

Characterisation	EU	US	Thailand
Name	Food supplements	Dietary supplements	Dietary supplements*
Category	Food	Food other than tobacco and conventional foods	Food other than conventional food
Substances	Single or combination of - Concentrated nutrients (vitamins and minerals) - Other substances (e.g. botanical, phytonutrients, enzymes, and essential fatty acids)	Single or combination of - vitamins, minerals, herb, other botanical, amino acid, amino acid	Single or mixtures - vitamins, amino acids, fatty acids, minerals, produces obtained from plants or animals - artificial substances imitated like above substances
Forms	- Dose form (e.g. capsules, pastilles, tablets, pills, sachets of powder, ampoules of liquids, drop dispensing bottles) - small unit quantities	concentrate, metabolite, constituent, or extract form	- in forms of tablets, capsules, powders, flakes, liquids or others which in not conventional form - concentrate, metabolite, constituent, or extract form
Purpose of consumption	Supplement to normal diet with nutritional or physiological effect	Supplement to total dietary intake by human	for benefit of health promotion

Remark: * Under unofficial translation, a word of "food supplement" is used in the notification of MoPH No.293 for English version, however, recently under ASEAN harmonization for health supplements, the word of "dietary supplement" is officially used instead.

From the above table, the definition of dietary supplements in Thailand seems to be modified from both EU and US since the regulation of dietary supplements was issued later than EU and US. Moreover, during the development of this regulation, definitions of food supplements from other countries such as Japan, Australia, EU and US were taken into account by the sub-committee on Nutrition and Nutrition &

[59] Clause 2 of the notification of the MoPH No. 293 B.E. 2548 (2005)
[60] Clause 3 of the notification of the MoPH No. 293 B.E. 2548 (2005)

Health Claims in order to address the definition of these products under the notification. Comparing to the definition of vitamin and mineral food supplements under the Codex standard (CAC/GL 55-2005), all of three definitions are comprehensively complied with the codex definition, however the scope of codex is narrower than three of them since the codex guideline is specifically issued for vitamin and minerals used as substances.

3.1.2 The borderline between food supplements and other similar products

In the view of definitions from three different regulations, a main meaning of either food supplements or dietary supplements is significantly similar that can be identified three special elements (Krutmann et al., 2011) in order to classify the product is a food supplement and distinguish it from medicinal, traditional product and other specific foods as follows:

1. Food Supplements are classified as food and regulated by food regulations. All measures applied to control food products shall be also implemented in food supplements. All relevant food laws clearly define food including food supplements significantly separate from medicinal products. In article 2 of the GFL, food shall not include medicinal products within the meaning of Council Directive 65/65/EEC and 92/73/EEC, and not include cosmetics within the meaning of Council Directive 75/768/EEC. Furthermore, in Article 2 of the Directive 2002/46/EC, only food supplements, except medicinal products, shall comply with this directive. Under the FD&C Act of US which has been amended by the DSHEA (Wollschlaeger, 2003), any dietary supplement is not a drug solely because of labelling contains such a claim whereas a truthful and not mislead food or dietary ingredient is not a drug under clause (U. S. FDA, 2004)[61]. Under the Food Act B.E. 2522 (1979) of Thailand, food is defined in section 4 which shall not include medicine, psychotropic, and narcotic substances. Under this aspect, food supplements can be considerably distinguished from medicinal products and, therefore, the medicinal law shall not be applied to food supplements.

2. Food supplements are intentionally consumed to supplement normal diet with nutritional or physiological effect for health promotion, neither for disease treatment nor prevention. If the product contains any substance providing properties on treatment disease, modification or correction related to disease, the substance or the product should be considered as medicinal type, not food supplements. From a purpose of use, food supplements can be defined separately from medicinal product and traditional medicines even the forms present similarly.

One well-known example on the borderline between food supplements and medicinal products related to nutritional or physiological property is the Case C-319/05 (EC, 2007b) judgment of the European court of Justice between the EC and the Federal Republic of Germany which is about garlic presentation in capsule form sold in Germany. The garlic capsule was classified as a medicinal product by German authority so it was required pre-market authorisation[62] . However, the European Court of Justice judged on 15 November 2007 that the garlic product is classified as a food supplement, not medicinal product because the effect on physiological functions is no more than the effects of a foodstuff consumed in a reasonable quantities and does not have a significant effect on the metabolism of restoring, correcting or

[61] Chapter II-Definitions (g)(1) of FD&C Act
[62] Article 6 of the Directive 2001/83/EC

modifying physiological function[63]. Moreover, the capsule form is not restricted to medicinal product. Therefore, the presentation in capsule form and daily consumption the garlic capsule containing 7.4 g of garlic which is in a corresponding amount in an appropriate manner with the normal diet may not be considered as a medicinal product. Similar to the garlic capsule case, herbal substances or extracts from herbal substances cannot be categorised as medicinal products if they are not presented for strictly treating or preventing disease in humans, or if they may not be administered to human being with a view to restoring, correcting or modifying physiological functions in humans (Chemist). Another problem on the borderline between food supplements and medicinal products is from the dose levels and product claims, e.g. glucosamine/chondroitin contained in food supplements with claim related to maintaining the health of joints, and generally has lower doses than drug products consisted by the same ingredients which, on the other hand, make claim related to reducing pain and stiffness associated with osteoarthritis (Krutmann et al., 2011).

Therefore, food supplements containing either a single or combination substances of vitamins, minerals, or herbal remedies are not classified as medicinal products, if they do not comply with the definition of the medicinal products and they do not provide higher doses and/or claims related to treating or preventing disease. However, in the EU, food supplements containing ingredients other than vitamins and minerals are not yet harmonised at the regional level but they are regulated by national law which can be various scopes country by country (Krutmann et al., 2011). According to the comparative study, the scope of this thesis focuses on vitamins and minerals supplements.

3. Food supplements are considered in concentrated form that present in small quantities and consumed other than conventional foods that categorising these products differ from other special foods such as novel food, Genetically Modified (GM) food, fortified food, and functional food by base on definitions and relevant regulations.

In the EU, a novel food is controlled under Regulation (EC) No. 258/97 which defines novel foods as food products and food ingredients that have not been used for human consumption to a significant degree within the EU before 15 May 1997 and fall in at least one of categories described in Article 1. By these categories, food supplements are excluded from novel food because the substances isolated from plants or animals are obtained by traditional propagating or breeding practices and having a history of safe food use, as well as the production process are currently used. However, some substances, especially in botanical supplements, do not have any history of use and the safety assessment may be concerned. In such cases, the substances would be classified as novel foods, if they have not been significantly used in EU prior to May 1997 (Coppens, Delmulle, et al., 2006). The GM food is regulated under Regulation (EC) No. 1829/2003 which determines definition of GM food under Article 2. Food supplements are not classified as GM foods if they do not contain ingredients from genetically modified organisms (GMOs). Food fortified with vitamins and minerals are specifically regulated under Regulation (EC) No. 1925/2006 which shall not apply to food supplements defined under the Directive 2002/46/EC[64]. For functional foods, even there is no specific definition in legal basis, they are regularly deemed as a food delivering a benefit to health beyond that of strict nutrition and making a claim of this benefit. Functional foods can be foods which are fortified with all kinds of ingredients to deliver a specific benefit to health (EAS, 2008) so that the scope of these products is extensively wider than food supplements by not only substances, quantities, but also forms of presentation.

[63] Article 1(2) of Directive 2001/83/EC
[64] Article 1(2) of the Regulation (EC) No. 1925/2006

The amount of intake and form of the functional food should be as it is generally expected for dietary purpose and as a part of the usual diet that are significantly different from food supplements which are typically marketed in the forms such as capsule, pill, powder or gel and not presented as a conventional food. Besides, rules and requirements applied in functional foods are very abundant depending on the nature of the foodstuffs (Siró, Kápolna, Kápolna, & Lugasi, 2008).

There is no special regulatory approval for novel food in the US if the constituents of the food are substantially similar to ingredients currently found in other foods (NCBE, 2006), on the other hand, the GM plants for food and feed are recognized under the Statement of Policy: Food Derived from New Plants Varieties (the 1992 policy) which is applied to all foods derived from new plant varieties through the recombinant deoxyribonucleic acid (rDNA) technology (U. S. FDA, 2012e). Foods including dietary supplements derived from plant varieties that are developed using rDNA technology are called "bioengineered foods" and should be complied with relevant policies and guidance. For fortification of food, US issues food fortification policies and provides code of Federal Regulations to establish a uniform set of principles that will serve as a model for the rational addition of nutrients to foods (U. S. FDA, 2012a)[65]. According to the US policy and guidelines, specific forms of presentation and quantification are not particularly determined for fortified foods, however the level of fortified nutrients should be limited based on the Reference Daily Intakes (RDI's). Similar to definition of functional food in EU, The Food and Nutrition Board of the National Academy of Sciences in US defines a functional food as "one of the encompasses potentially healthful products, including any modified food or food ingredient that may provide a health benefit beyond that of the traditional nutrients it contains" (Milner, 2000) which is more comprehensive aspect than dietary supplements. There is lack of a legal requirement on functional foods (Milner, 2000), however, functional foods are generally controlled as one kind of conventional food products by all general provisions of the FD&C Act while the dietary supplements are subjected to particular provision of the DSHEA that do not apply to conventional foods, including the functional foods (Taylor, 2004) resulting in obvious differentiation between functional foods and dietary supplements.

Unlike EU and US, in Thailand, novel and fortified foods are not controlled by specific regulations but relevant regulations are implemented to control safety and quality aspects such as nutrition labelling, nutritional and health claims, and food additives. Furthermore, criteria and implementation guideline for Nutrification (T. FDA, 1995) defined as any food which is fortified by one or more than one nutrients for enhancement of nutrition value have been issued in order that vitamins or minerals added into traditional foods are based on the safety level and the Thai Recommend Daily Intakes (Thai RDI). Apart from these special foods, the GM foods obtained ingredients or produced through certain techniques of Genetic Modification/Genetic Engineering shall be complied with the notification of the MoPH No. 251 (T. FDA, 2002).

From the views of laws in EU, US and Thailand, classification of product as a food supplement or medicine depends on its intended use including information and presentation of the product decided by FBOs. Comparing to drug, food supplements mainly offer health benefits but not for disease treatment or prevention as well as dose form and quantities for consumption are significantly important to distinguish between food supplements and the other foods. Therefore, In cases of confusion to categorise a product whether it is food supplement or medicine, definitions indicated under relevant laws are functionally used for the classification, however, they are not fully applied in every case and some situations need to be

[65] Fortification Policy Statement of Purpose CFR §104.20

solved case by case (Krutmann et al., 2011). An example for a complex product is a concentrated tomato juice which has and increased concentration of folic acid (Vitamin B9) and Vitamin C. This beverage may be defined as a fortified product whereas it can be classified as food supplements if its label presents word of "food supplement" and an intake dose level (Petroczi et al., 2011).

For a simple case of borderline product classification, a decision tree for the classification of food supplements as Food or Medicinal products published by the Government Chemist(Chemist) has been modified based on above information as follows:

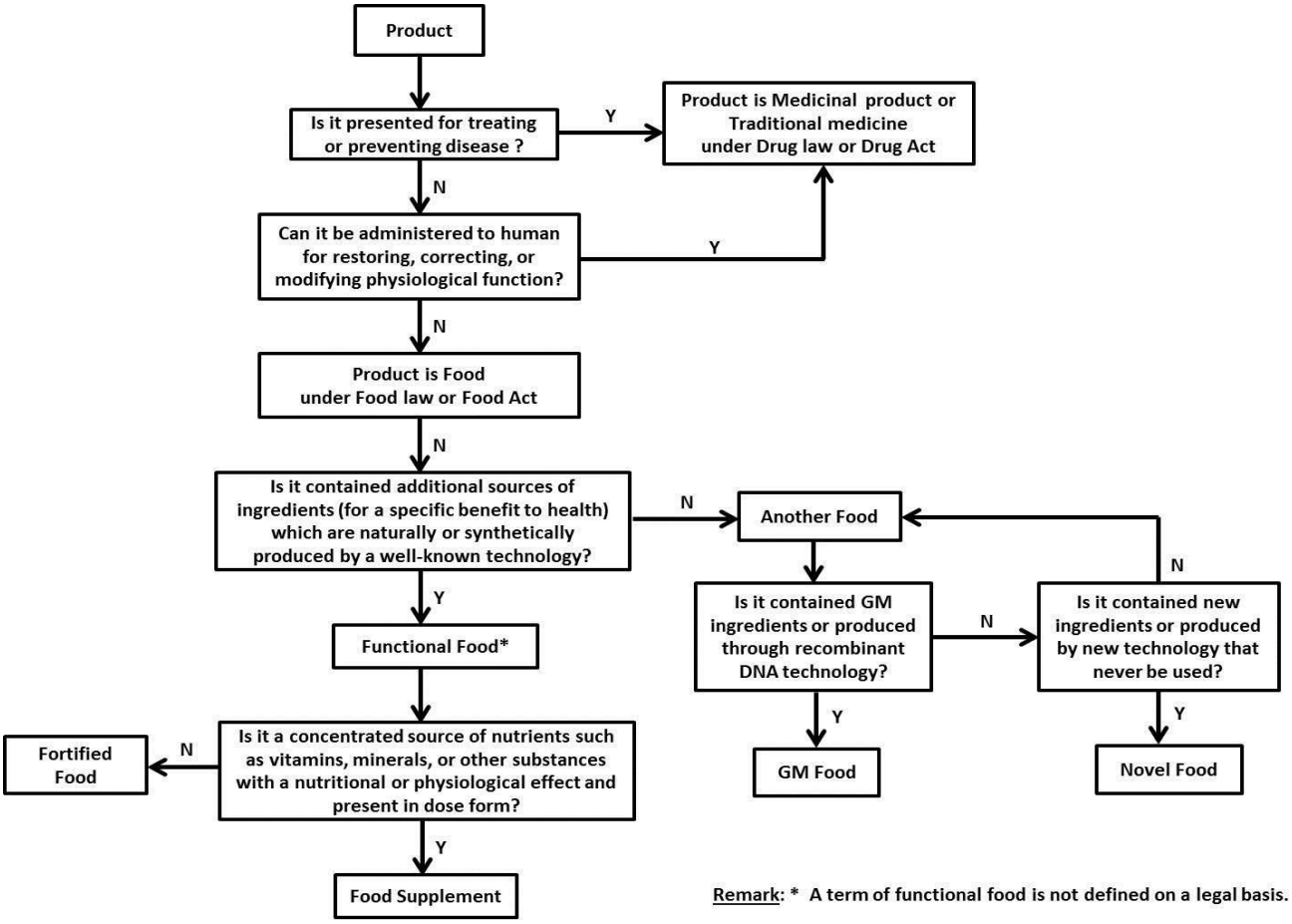


Figure 7 Decision tree for the classification of food supplements[66]

3.2 Regulations and Pre-market control systems

How are food supplements controlled safely for consumers is one of key questions in this thesis. EU, US, and Thailand regulate and manage food supplements based on international guidelines, the risk analysis principle, and scientific evidence, but the national/regional requirements may differ depending on consumption data, nutrition value for domestic population, consumer awareness on these products, and other factors affecting law development, especially in social and economic aspects. Even the regulations may

[66] Modified from the Government Chemist(Chemist),p.8

provide different measures, the major objectives of legislation and enforcement in EU, US, and Thailand are mostly comparable in order that food supplements comply with relevant requirements on safety and efficacy, whereas consumers are confident in having freedom of choice to purchase any food supplement with the reliable information.

From point of view, the regional and national regulations for food supplements focusing on vitamins and minerals are generally comprehensive into "**three P (3Ps)**" perspectives; **P**roducts, **P**remises , and **P**resentations which can be elaborated separately by each region or country as follows:

3.2.1 EU: Regional and national systems

Vitamins and minerals contained in food supplements are initially controlled based on the Directive 2002/46/EC for harmonization among MSs (Coppens, Da Silva, et al., 2006). Only vitamins and minerals listed under Annex I and II of this directive can be marketed as food supplements in the EU[67] and requirements for these micronutrients mainly focused on this thesis are as follows:

3.2.1.1 REQUIREMENTS OF PRODUCT PERSPECTIVES

1) The positive List and new substances

According to the directive 2002/46/EC, allowed types and forms of both vitamins and minerals are listed in Annex I and II, respectively. This positive list that had been scientifically evaluated by the EFSA based on safety and bioavailability assessment provides advantages to relevant stakeholders. It helps not only to ensure that micronutrients are safe for consumer health, to facilitate FBOs who would like to produce and/or sale food supplements without pre-market authorisation if the vitamins and/or minerals contained in the products comply with the positive list, but also to support competent authorities of MSs to enforce and monitor these products. In contrast, any food supplement consisting of micronutrients that exclude from the positive list shall be legally prohibited to be placed on the EU market[58]. For other substances, the EC by coordinating with MSs and EFSA is requested to submit a report on the suitability of establishing specific rules to the European Parliament and the council by not later than 12 July 2007. It aims to be a second step of harmonisation process on food supplements among MSs of EC (Coppens, Da Silva, et al., 2006).

By enforcing this directive, there is a wide gap of micronutrients currently used in food supplements but have not evaluated safety aspect by EFSA. This directive under Article 6, hence, provides derogations to MSs until 31 December, 2009. Vitamins and minerals which are not in the positive list can be used in the food supplements as long as the following conditions are fulfilled:

a) The substances in question are used in one or more food supplements marketed in the Community on the date of entry into force of this directive or prior to 12 July 2002.

b) The EFSA has not given an unfavourable option in respect of the use of the substance, or its use in that form, in the manufacture of food supplements, on the basis of a dossier supporting use of the substance that has to be submitted to the EC by the MSs not later than 12 July 2005.

[67] Article 4 of the Directive 2002/46/EC

With new scientific evidences, scientific information submitted by MSs, and technology development, the positive list of vitamins and minerals shall be regularly modified and published in new directives and regulations (EC, 2012c) as below table:

Table 2 Summary of relevant directives and/or regulations with improvement of the positive list of vitamins and minerals applied in food supplements under EU markets.

Directive/Regulation	Summary of amendment
Directive 2006/37/EC	Annex II of Directive 2002/46/EC had been modified as described in the Annex (Article 1) by; 1) In Section A, to replace the heading "10. Folic Acid" by "10. Folate" 2) In Section A, to add "(b) calcium-L-methylfolate" under heading 10. 3) In Section B, to insert "ferrous bisglycinate" before "cupric carbonate"
	MSs shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive by 30 April 2007 and then inform to the EC (Article 2)
Regulation (EC) 1170/2009	Annexes I and II of Directive 2002/46/EC are replaced respectively by the texts in Annex I and II to this regulation (Article 1)
	This Regulation shall be directly applicable in all MSs and it shall enter into force on the 20th day following its publication in the Official Journal of the European Union (Article 3)
Regulation (EC) 1161/2011	Annex II of Regulation (EC) 1170/2009 had been modified as described in the Article 1 by; 1) In Section B, to insert "ferrous ammonium phosphate" and "ferric sodium EDTA" after the entry "ferrous phosphate" 2) In Section B, to insert "sodium sulphate" and "potassium sulphate" after then entry "sodium salt of orthophosphoric acid"
	This Regulation shall be directly applicable in all MSs and it shall enter into force on the 20th day following its publication in the Official Journal of the European Union (Article 4)

From 1st January 2010, only micronutrients which are assessed for safety and bioavailability evaluation by EFSA and listed in the positive list can be continuously used in food supplements (EFSA, 2009a). In case of new vitamins and minerals that are not included yet in the positive list, scientific dossiers concerning on the safety and bioavailability of the individual substance shall be submitted to EFSA for further assessment and adoption to the positive list. To comply with this requirement, the EC publishes "Guidance on submissions for safety evaluation of sources of nutrients or of other ingredients proposed for use in the manufacture of foods" developed by the EFSA and "Administrative guidance on submission for safety evaluation of substances added for specific nutritional purposes in the manufacture of foods" which covers to food for particular nutritional uses, fortified food, and food supplements that are available on the EC Website (EC, 2012c). A submission procedure particularly in food supplements based on these guidelines is summarised as three following steps:

Step 1: Document preparation responsible by a petitioner. Documents needed for submission can be mainly classified as 2 parts as

1) A letter of application with clearly specifying name of new substance required for safety evaluation and addressing the related directive for its application (Directive 2002/46/EC for food supplements); and

2) A technical dossier consisting of 5 elements 1) administrative data, 2) technical data, 3) biological and toxicological data, 4) Sources, and 5) Annexes. The documents for each part are listed in Annex I of this thesis.

An electronic version of the letter, a copy of the summary document and a copy of the full technical dossier should be sent by registered post to the office of DG Health and Consumers, EC.

Step 2: Follow up of a petition. Whenever the Commission service of DG Health and Consumer receives the application, an acceptation letter with a reference number and name of nutritional substance(s) requested to get approval for further correspondence will be sent to the petitioner. There are two possible responses from the Commission services

1) Asking for more information. In this case, the Commission services may decide to do not administratively accept the application yet, but will directly inform the petitioner about name of information or data additionally needed for consideration and permission.

2) Acceptation. When all data is reviewed and administratively accepted by the Commission service, the petitioner will be confirmed and asked to submit the full application to the Secretariat of the Scientific Panel of Food Additives and Nutrient Sources added to Food of the EFSA with copies of following documents by registered post.

Table 3 List of documents for full application on safety evaluation of new substances.

Document	Number of copies
1. the letter specifying the request	1
2. summary of technical dossier	3
3. Full dossier	3
4. Full information in electronic format (on standard physical media, e.g. CD-ROM or equivalent)	1

In a case that EFSA asks for additional information or sections of the dossier to additional addresses as further complete assessment, the applicant should readily submit the requested document in paper and electronic formats to both EFSA Secretariat and the Commission services. It also would be remarked that a confidential submission cannot be accepted according to these guidelines. Therefore, a confidential section should be clearly marked as such and kept to a minimum as well as the applicants are encouraged to make publicly available a maximum of the information submitted, for example by posting on the Internet the contents of the application.

Step 3: Safety evaluation by existing Panel on additives and nutrient sources added to food (the ANS Panel) under EFSA. Two aspects are mainly considered for risk assessments; safety of micronutrients sources and bioavailability of the substances such as absorption of the micronutrients in the human body. In the process of evaluation, if the dossiers show insufficient scientific evidences, they can be withdrawn and rejected to add in the positive list. Between 2005 and 2009, 533 applications relating to 344 different substances were examined by EFSA; however only 39 applications were possibly concerned based on the safety and bioavailability criteria because 186 applications were withdrawn during the evaluation process while half of the remaining applications were inadequate scientific data (EFSA, 2009a). Finally, the adopted opinion on the substances will be publicly available on the EFSA websites.

One example of EFSA scientific opinion on safety evaluation of a new substance for food supplement is vitamin B_{12}-enriched yeast for nutritional purposes (EFSA, 2009b)[68]. EFSA was requested by EC since 2005 to provide a scientific opinion of safety of vitamin B_{12}-enriched yeast which is derived from specified strains of *Saccharomyces cerevisiae*. According to dossiers provided by the petitioner, vitamin B_{12} is naturally integrated by the growing yeast into its own structure and occurs to be present in any food material. Even the *Saccharomyces cerevisiae* has a quantified presumption of safety and vitamin B_{12} from the vitamin B_{12}-enriched yeast is safe, the EFSA provided opinion that the vitamin B_{12}-enriched yeast cannot be assessed based on safety and bioavailability aspects because no data was provided on the bioavailability of vitamin B_{12} from the vitamin B_{12}-enriched yeast and insufficient evidence to demonstrate that the vitamin B_{12} complex formed within eukaryotic cells have a metabolic fate and biological distribution similar to those of other sources of vitamin B_{12} in the diet. By this example, it has been shown that EFSA works to confirm that the sources of vitamins and minerals used in food supplements sold in the EU are safe and can effectively provide these nutrients to the human body; however, Time-consuming for completing safety evaluation on a new substance is a barrier to product development.

2) Maximum safe level of vitamins and minerals

Aside from vitamins and minerals substances established in the positive list, the Standing Committee on Food Chain and Animal Health of EC shall establish minimal and maximum levels in food supplements by scientific risk assessment based on generally accepted scientific data, various degrees of sensitivities of different consumer groups (Article 5 of the directive 2002/46/EC) in order to prevent consumers from overdose intake resulting in adverse effect (CBI, 2012a). There are 2 major phases working on maximum safe level establishment for vitamins and minerals on risk analysis principle (Coppens, Da Silva, et al., 2006).

Phase 1: ULs of the vitamins and minerals are initially set for general population by the EFSA. The ULs of a micronutrient is the maximum intake level that can be consumed daily over lifetime without being likely to pose any risk to health according to available evidence. Each vitamin and mineral is evaluated on risk and safety associated with chronic daily intake from all sources and the ULs of the micronutrients were published (Flynn et al., 2003). In 2006, the ULs of 34 micronutrients were reviewed and published (EFSA, 2006). According to this report, the ULs were estimated as the highest level of intake, not a recommended level, for all groups of the general population based on scientifically nutritional data and risk assessment process (see in Annex II).

[68] Scientific opinion (Question No EFSA-Q-2005-195), adopted on 4 June 2009.

Phase 2: The Maximum levels of micronutrients used in food supplements will be considerably set up based on established ULs proposed by the EFSA and intake level of vitamins and minerals from other food sources including water. There are various risk management models proposed for establishing the maximum levels; the Danish budget model developed by the Danish Institute of Food and Veterinary Research, the ERNA model developed by the European Responsible Nutrition Alliance (ERNA) and another similar model proposed by the International Life Science Institute (ILSI) (EC, 2012c). A draft proposal for a harmonised regulatory framework on the addition of vitamins and minerals to food supplements is proposed that the supplement users will be protected by a number of measures, including the setting of maximum safe limits of nutrient content together with provision of information through labelling and claims (Flynn et al., 2003). The EC acting as a risk manager published a discussion paper on the setting of maximum and minimum vitamins and minerals in foodstuffs (EC, 2006) including food supplements which is circulated to both MSs and relevant stakeholders for their response. Comments and responses have been submitted and reviewed by the EC for further discussion and finalisation of the maximum and minimal levels for micronutrients contained in food supplements. According to up-to-date status of process, the final decision on establishment of maximum and minimum amounts of vitamins and minerals in foodstuffs and food supplement is not yet achieved.

3) Other safety requirements for product perspective

Since the food supplements are classified as food under the Directive 2002/46/EC, all requirements and revisions for food are automatically applied to control level of safety. Apart from general requirements under the GFL such as responsibilities, traceability, recall and emergency response, other horizontal regulations related to foods are also legally implemented (Silano, Coppens, Larrañaga-Guetaria, Minghetti, & Roth-Ehrang, 2011) to ensure that unsafe food shall not be placed on the market[69]. Main regulations relevant with food and food supplements can be concluded as follows:

1. Regulation (EC) 1881/2006 on setting maximum levels for certain contaminants in foodstuffs. Types of contaminants, maximum level and groups of foodstuffs are set up in the annex of this regulation to ensure that the foodstuffs listed in the annex shall not be placed on the market where the level contaminants contained in these foodstuffs exceed the maximum limit described in this annex. Contaminants and maximum level addressed in this regulation are such as Nitrate, Mycotoxins, Metals, 3-monochloropropane-1,2-diol (3-MCPD), Dioxin and PCBs, and Polycyclic aromatic hydrocarbons.

2. Regulation (EC) 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin. Maximum Residue Limits (MRLs) in products of plant and animal origin or parts used as fresh, processed and/or composite food are established under the Annex I of this regulation. MRLs for processed food are generally calculated based on the MRLs for the agricultural products with consideration on appropriate dilution or concentration factor whereas, for composite foodstuffs, the relative concentrations of the ingredients in food are significantly taken into account for the calculation (Meulen B.M.J. van der, 2008). Under Annex II, specific MRLs for food or pesticide combination are set up, while temporary MRLs and a list of active substances which are not required MRLs due to no pose a health risk are established in Annex III, and IV respectively.

[69] Article 14 of the Regulation (EC) No. 178/2002

3. Council Directive 89/107/EEC concerning food additives authorised for use in foodstuffs intended for human consumption. In case that a food additive is needed for a technological purpose but not added to foodstuffs as nutrients such as minerals, trace elements or vitamins, only the food additives listed in Annex I can be legally applied into foodstuffs. Any food additive which is not addressed in the list, pre-market authorisation is required. After approval, an E number will be given and used to draw up the ingredient list on the label of food product. Moreover, food additives such as sweeteners, colours, and other miscellaneous additives are controlled by specific directives, namely Directive 94/35/EC, Directive 94/36/EC, and Directive 95/2/EC, correspondingly (Meulen B.M.J. van der, 2008).

4. Regulation (EC) 2073/2005 on microbiological criteria for foodstuffs. This regulation includes not only microorganisms, their toxins, but also metabolites with the general and specific hygiene measures[70]. FBOs shall ensure that foodstuffs are complied with the relevant microbiological criteria for *Listeria monocytogenes*, Salmonella, *Staphylococcal* enterotoxins, *Enterobacter sakazakii*, *E.coli* and histamine[71]. Process hygiene criteria for some certain food products as well as rules for sampling and preparation of test samples are described under the Annex[72].

5. Regulation (EC) 1935/2004 on food contact materials, which is one of general requirements applied to all foods including food supplements. By this regulation, 17 groups of substances used for producing food contact materials are controlled by specific measures, such as plastics, waxes, regenerated cellulose, metals and alloys, paper and board. It shall ensure that components of food contact materials must not transfer into food in quantities that could endanger human health, change compositions of food in an unacceptable way or deterioration of taste and odour of food (EC, 2012b). Specific regulations are also enacted for a particular food contact material such as Regulation (EU) 10/2011 on plastic materials and articles intended to come into contact with food which covers to all packages made or consisted of plastics including plastic layers or plastic coating, forming gaskets in caps and closures. The union list of authorised substances used in plastics is developed in Annex I as a positive list to control that only these permitted substances and components can be legally used in the manufacture of plastic materials and articles.

3.2.1.2 REQUIREMENTS OF PREMISES PERSPECTIVES

The Regulation of food hygiene (EC Regulation 852/2004) plays an important role on controlling quality and safety of food production and facilities to produce food including food supplements (EC, 2006; Krutmann et al., 2011) at all stages of the food chain including exports[73]. Apart from this hygiene regulation, there is a more specific hygienic rule for food of animal origin called "Regulation (EC) 853/2004" which implements to both unprocessed and processed products. By collaborating with the EC and MSs, FBOs are mainly responsible to register their food establishments and ensure that all stages from production to delivery are under control satisfy the relevant hygiene rules which can be concluded, specifically for food supplements, as follows:

[70] Article 4 of Regulation (EC) No. 852/2004
[71] Chapter 1 of the Annex I of the Regulation (EC) No. 2073/2005
[72] Chapter 2 and 3 of the Annex I of the Regulation (EC) No. 2073/2005
[73] Article 1(g) of the Regulation (EC) No. 852/2004

Table 4 Summary of general hygiene requirements for food supplements

Step	Responsibilities by FBOs	Responsibilities by EC and MSs
Production	- Comply general requirements based on HACCP principles described in Annex II - Implement specific hygienic requirements for food of animal origin based on Regulation (EC) 853/2004 - Apply for the registration or approval on food establishments - Comply with microbiological criteria, temperature control requirements, and cold chain maintenance, as applicable - Implement sampling and analysis - Prepare records and results of analysis which are readily available submit to the competent authorities when they ask.	- Develop guides both national and community levels to good practices for hygiene and the application of HACCP principles and disseminate to FBOs - Register and/or approve the food establishments based on national official control and competent power under both the Regulation (EC) 882/2004 and the Regulation (EC) 854/2004, particularly in food products of animal origins.
Distribution and transportation		

Apart from HACCP based procedure, voluntary guides on GMP are also developed by MSs and the EC[74] to support FBOs as an aid to comply with obligations under this regulation[75].

3.2.1.3 REQUIREMENTS OF PRESENTATION PERSPECTIVES

In article 14 of the GFL, food shall not be placed on the market if it is unsafe which regards to the normal conditions of use, and information provided to the consumer including information on the label, or other information available to the consumer. Presentation of food including labelling, advertising related to food shall not deceive consumers[76]. Therefore, food supplements shall not be placed on the market if the information provided through package label, claims, or advertisement mislead to consumers. To avoid misleading information, FBOs shall comply with following legal requirements:

1) Labelling

A labelling which defines to any words, particulars, trademarks, band name, pictorial matter or symbol relating to a foodstuff and placed on any packaging, document, notice, label, ring, or colour accompanying or referring to such foodstuff shall be complied with the Directive 2000/13/EC[77]. Apart from these general requirements, labelling for food supplements shall be followed by particular rules addressed in the Article 6 –10 of Directive 2002/46/EC. This following information must be included in the product labels:

1. The word of "food supplement"

2. The names of the categories of nutrients or substances that characterize the product

[74] Article 7-9 of the Regulation (EC) No. 852/2004
[75] Article 4(6) of the Regulation (EC) No. 852/2004
[76] Article 16 of the Regulation (EC) No. 178/2002
[77] Article 1(2) of the Directive 2000/13/EC

3. The portion of the product recommended for daily consumption (Recommended Daily Allowance, RDA). The numerical units shall be declared following available reference in Annex I of the directive

4. A warning not to exceed the stated daily dose

5. A statement of the effect that food supplements should not be used as a substitute for a varied diet

6. A statement of the effect that the products should be stored out of the reach of young children

Figure 8 An example of a label for vitamin B capsules based on EU specific requirements (CBI, 2012a)
(The red numbers correspond with above particular requirements for food supplements)

The labelling of supplements including presentation and advertisement shall not include any mention implying that a balance and varied diet cannot provide appropriate quantities of nutrients in generals while claims on the label shall not refer to prevent, treat or cure human disease. FBOs shall declare nutrients values based on analytical results of that supplement, however, the nutrition labelling is not legally required for food supplements[78].

2) Claims

All nutrition and health claims made in commercial communication through whether in the presentation, labelling or advertisement to reach final consumers shall be complied with the Regulation (EC) No 1924/2006 addressing a claim as any message or representation, which is not mandatory under Community or national legislation, including pictorial, graphic or symbolic representation, in any form, which states, suggest or implies that a food has particular characteristics [79]. A nutrition claim implies to food which has particularly beneficial nutritional properties due to provide or contain energy and/or nutrients or other substances while a health claim refers to a relationship exists between food or its constituents and health. Both of claims shall only be permitted to use if they are fulfilled with sufficiently scientific evidence, nutrient profile compliance, and accurate understanding from average consumers. The number of average consumers is not based on statistical system but considered by national courts and authorities (Reuterswärd, 2007).

[78] Article 1 (2) of the Council Directive 90/496/EEC
[79] Article 1 and Article 2 (2) of the Regulation (EC) No. 1924/2006

In the particular requirements, permitted nutrition claims are listed in the annex of this regulation adopted by the EC after consultation with the EFSA and interested stakeholders[80]. In practical terms, the wording used in the annex could be different from the list but it should be subjected to the same conditions of use indicated therein such as 'with…', 'added….', or 'enriched…' are used the same condition with 'source of….'. Examples of nutrition claims (Verhagen, Vos, Francl, Heinonen, & van Loveren, 2010) are 1) content claims implying to a level of a nutrient contained in a food; and 2) comparative claims referring to compare nutrients and/or energy value of two or more food which is a same range of food category[81].

From specific conditions of health claims, function claims are related to health benefits for 1) growth, development, and the functions of the body; or 2) psychological and behavioural functions; or 3) weight control or increase in the sense of satiety or to the reduction of the available energy from the diet. However, there are two different procedures for function claims depending on scientific substantiation (Reuterswärd, 2007). In case that "generally accepted scientific evidence" and "the claim is well understood by the average consumer" are applied to support a health claim, the claim will be classified in Article 13.1 and shall be adopted in a Community list[82]. The "Article 13.1 claims", therefore, may be made without full authorisation[83]. On the other hand, if there is "newly developed scientific evidence" used for making a health claim, it may be categorised in Article 13.5 which is not included in the Community list so that the procedure addressed under Article 18 shall be applied. In case of health claims implying to reduction of disease risk claims and the children's development[84], dossiers related to scientific proved on safety shall be submitted following the relevant procedures[85] including an EFSA guidance "scientific and technical guidance for the preparation and presentation of the application for authorisation of a health claim" in order to be listed in the Community Register. Under the EFSA guideline for health claims, "wording" used in the claims is essentially mentioned in order that the wording and the presentation of health claim are clear, reliable, and truthful for consumers (Reuterswärd, 2007). There are some restrictions of the use of health claims[86] such as 1) claims which suggest that health could be effected by not consuming the food; 2) claims which make reference to the rate or amount of weight loss; and 3) claims which make reference to recommendation of individual doctor or health professional and other association not included in Article 11. In addition, the health claims are prohibited if they refer to the prevention, the treatment or the cure of a human disease[87] such as "this supplement can prevent stomach cancer" (Verhagen et al., 2010).

Nutrition and health claims used in food supplements shall comprehensively comply with not only this regulation, general requirements in the GFL, but also specific requirements addressed in the Directive 2002/46/EC. It is also important to know composition data in the food supplements in order to verify that its nutritional composition is present in sufficient quantities to make the relevant claims (Buttriss & Benelam, 2010). For new claims, they will be rejected, unless they can fully comply with these criteria: 1) safe (no adverse effect); 2) no change brought to desirable eating patterns; 3) not misleading; and 4) beneficial.

[80] Article 8 of the Regulation (EC) No. 1924/2006
[81] Article 9 of the Regulation (EC) No. 1924/2006
[82] Article 13 (3) of the Regulation (EC) No. 1924/2006
[83] Article 15-19 of the Regulation (EC) No. 1924/2006
[84] Article 14 of the Regulation (EC) No. 1924/2006
[85] Article 15, 16, 17, 19 of the Regulation (EC) No. 1924/2006
[86] Article 12 of the Regulation (EC) No. 1924/2006
[87] Article 2 of the Directive 2000/13/EC

The authorisation process is provided for the new claims with interaction between the applicant, MSs, EFSA, EC, and public consumers before the approved clams will be listed in the "Community Register of nutrition and health claims made of food" which is regularly revised (Cheftel, 2005). Summary of the claim approval process and examples of permitted nutrition and health claims to food including food supplements are showed in below flowchart and table, respectively:

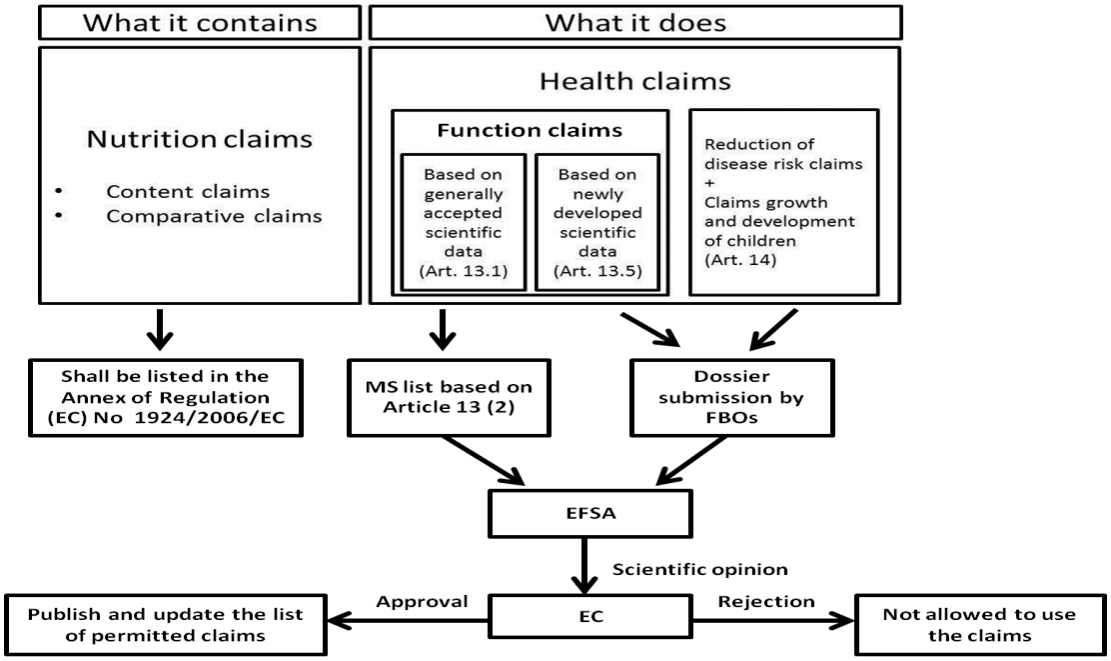


Figure 9 Summary of the claims approval process (Buttriss & Benelam, 2010; Verhagen et al., 2010)

Table 5 Examples of permitted nutrition and health claims

Type of claim	Example of claim	Remark
1. Nutrition claims		- under the Annex of Regulation EC No 1924/2006
1.1 Content claims	Source of Vitamin C	
1.2 Comparative claims	High Vitamin C	
2. Health claims		
2.1 Function claim		
- Art. 13.1 claims	Vitamin E protect the fat in body tissues form oxidation	- under the Community list or;
- Art. 13.5 claims	Function claim with "emerging evidences"	- apply for claim approval following the procedure in Article 18
2.2 reduction of disease risk claims and the children's development	Calcium and/or Vitamin D can reduce a risk of osteoporosis disease Vitamin D is needed for the normal growth and development of bone in children	- apply for claim approval following the procedure in Article 15,16,17, and 19

3) Advertisement

In general, the Directive 2006/114/EC concerning misleading and comparative advertising legally entered into force on 12 December, 2007 to protect traders and consumers against misleading advertising as well as to lay down the condition of authorised comparative advertising for preventing internal market from distortion of competition. Based on definitions[88], an advertisement covers to all presentation forms connected with a trade, business, craft or profession in order to promote the supply of goods or services. It shall also apply to community provision on advertising for specific products and/or services to restriction or prohibits on advertising in particular media[89]. Two major advertising criteria have been set based on this directive:

1. Misleading advertising is prohibited. The misleading advertising covers to any advertising including its presentation deceives or likely to deceive the persons to whom it is addressed or it reached and which, by reason of its deceptive nature, is likely to affect their economic behaviour or injures or is likely to injure a competitor. The misleading nature of advertisements depends on following criteria[90]:

- The characteristics of the goods or services such as availability, nature or composition, method of manufacture or provision, origin, etc. It includes the results to be expected from their use, and the results of quality checks carried;

- The conditions governing the supply of the goods or services;

2. Comparative advertising which means any advertising which explicitly or by implication identifies a competitor or goods or services offered by a competitor shall be only permitted if it is not misleading and complied with following conditions[91];

- Relate to goods or services which meet the same needs or are intended for the same purpose;

- Relate to products with the same designation of origin;

- Avoid creating confusion between traders, and should not discredit, imitate or take advantage of the trade mark or trade names of a competitor.

MSs shall ensure that those persons or organisations with a legitimate interest may bring a court action or an administrative appeal against illicit advertising[92] by providing preventive measures such as withdrawal of illicit advertising, even in the absence of proof, of actual loss, damage or of an intention of negligence, or prohibition of illicit advertising which has not yet been published. For food supplements, an advertisement is particularly controlled by both requirements of the product label and claims.

[88] Article 2 of the Directive 2006/114/EC
[89] Article 8 of the Directive 2006/114/EC
[90] Article 3 of the Directive 2006/114/EC
[91] Article 4 of the Directive 2006/114/EC
[92] Article 5 of the Directive 2006/114/EC

3.2.1.4 SPECIFIC REQUIREMENTS AT NATIONAL LEVEL: IRELAND CASE STUDY

All MSs shall control food supplements according to the Directive 2002/46/EC[93] and they may also regulate additional restrictions to implement under a national level[94]. By overview of all 27 MSs implementing directive and regulations in relation to food supplements (CBI, 2012b), there are only three MSs have completely harmonised national regulations according to the EC directive 2002/46/EC; Austria, Sweden, and UK. Other MSs have established derivative requirements such as national maximum and minimum levels for certain vitamins and minerals in Denmark, France, Finland, and the Netherlands, or notification of placing a food supplements for the first time in Germany, Ireland, Italy, and Spain. Because of a language obstacle for accessing information and interesting derivation between national requirements and regional directive, regulations of food supplements in Ireland are selected for comparative study at national level in this thesis.

European Communities (Food Supplements) Regulations 2007 (S.I. No. 506 of 2007) is a principal provision to control food supplements placed in an Irish market. This provision was revised by the European Communities (Food Supplement) (Amendment) Regulations 2010 (S.I. No. 355 of 2010) which shall be construed together with the principal regulations 2007 as one (FSAI, 2010b)[95]. Requirements and measures under these regulations apply to all stakeholders relevant with supply chain of supplements; covering from manufacturers, importers, distributor, and retailers including website sale, direct sale and network marketing (FSAI, 2010d). Manufactures are mainly responsible for domestic supplements while importers are in charge of imported supplements including the products sold via internet which shall be fully complied with the provisions. These regulations also apply to the supplements intended for exporting outside the EU whether or not they are sold in Ireland, unless the products that do not comply with this provision may be exported outside the EU if they meet the following criteria (FSAI, 2010d):

1. The competent authorities of the importing country have expressly agreed to this importation, after having been fully informed the reasons for which and the circumstances in which the concerned food supplements could not be placed on the Irish market; and

2. The products are not injurious to health.

Under Part 1 of the provision 2007, responsibilities of relevant competent authorities are clearly identified. The FSAI acts as a regulatory body and a contact point of Ireland to other MSs, the EFSA, and the EC as well as considers on the notification procedure of food supplements. Enforcement of the regulations is also responsible by the FSAI which is carried out by the official agency such as Health Service Executive (HSE) and official laboratories referring to the Public Analyst's Laboratory in Cork, Dublin, or Galway.

Three perspectives relevant with food supplements in Ireland are analysed as follows:

1) Product Perspective

Most of contents in the provisions are complied with the EC directive 2002/46/EC; for examples, scope of provision, purity criteria of substances, and positive lists provided in Schedule 1 and 2 (FSAI,

[93] Article 3 of the Directive 2002/46/EC
[94] Article 4(7) of the Directive 2002/46/EC
[95] Regulation 2 of the S.I. No. 355 of 2010

2007)[96] and updated in the provision 2010 to align with updated EC directives. Only substances listed in the schedules can be used in supplements and they shall not be considered either novel foods or medicinal products which exerts a pharmacological action[97]. In case of unclear classification between supplements and medicines, the FSAI will liaise with the Irish Medicine Board (IMB), a competent authority for medicinal products in Ireland, and the individual FBO on case-by-case basis. When the maximum and minimum levels for micronutrients are adopted by the EC, they will be also applied to supplements sold in Irish market.

Comparing to the EC Directive 2002/46/EC, two special requirements have been set up to implement in a compulsory basis. Firstly, the notification procedure is required[98] when the product is produced in or imported into Ireland and is being placed on the Irish market for the first time by an individual sector (e.g. manufacture, distributor, importer, or retailer), irrespective of product country of origin (FSAI, 2010d), while different flavours of supplements shall be separately notified. The notification must be accompanied by a model of the product label including relevant literatures with the product (Cox, 2010). It has been clearly addressed that the notification procedure is not an approval or authorisation procedure but it helps to facilitate efficient monitoring of all supplements sold in Ireland (FSAI, 2010d). The notification shall be submitted to the FSAI through "the online notification system"[99] with some certain information regarding the products such as product name, manufacturer/importer name and address, product description, a copy of product label, etc. Once the notification has been submitted, a reference number of the product will be automatically generated as a reference for any correspondence with the FSAI. After receiving these notifications, the FSAI regularly checks compliance of the notification with relevant regulations as well as sends FBOs a letter acknowledging receipt of the notification, advice of legal responsibilities related to food supplements, or outlining of rejection matter, in case of unacceptable issue in a product notification. Besides, the FSAI may request FBOs additional information to ensure the supplements are complied with specific requirements and relevant regulations. The submitted notification can be revised if the product has been reformulated (e.g. change in ingredients, or amount of nutrients) through the online system, however, revised product shall be applied a new submission in case that the notification has been notified to the FSAI prior to 2010. All information submitted through this network system will be confidentially kept by the FSAI and only the list of notified food supplements will be provided to the HSE office via "the Safety Net", an internal system served to official agencies for further enforcement and monitoring in the market.

In case of importing food supplements that contain a product of animal origin, additional notification and registration requirements shall be applied to the Department of Agriculture and Food (DAF). The procedures may implement differently depend on the products imported from EU country or a non EU country (Cox, 2010).

Secondly, enforcement procedure has been established[100] that sets up a sampling procedure for food supplements, responsible agencies, timeline, criteria of non-compliance, and punishments.

[96] Part 1 – 2 of the S.I No. 506 of 2007
[97] Regulation 3(2) of the S.I No. 506 of 2007
[98] Regulation 6 of the S.I No. 506 of 2007
[99] Available at https://supplements.fsai.ie/
[100] Part 3 of the S.I No 506 of 2007 and updated by the S.I. No. 355 of 2010

From additional measures on food supplements in Ireland, the procedure can be summarised as below flow chart;

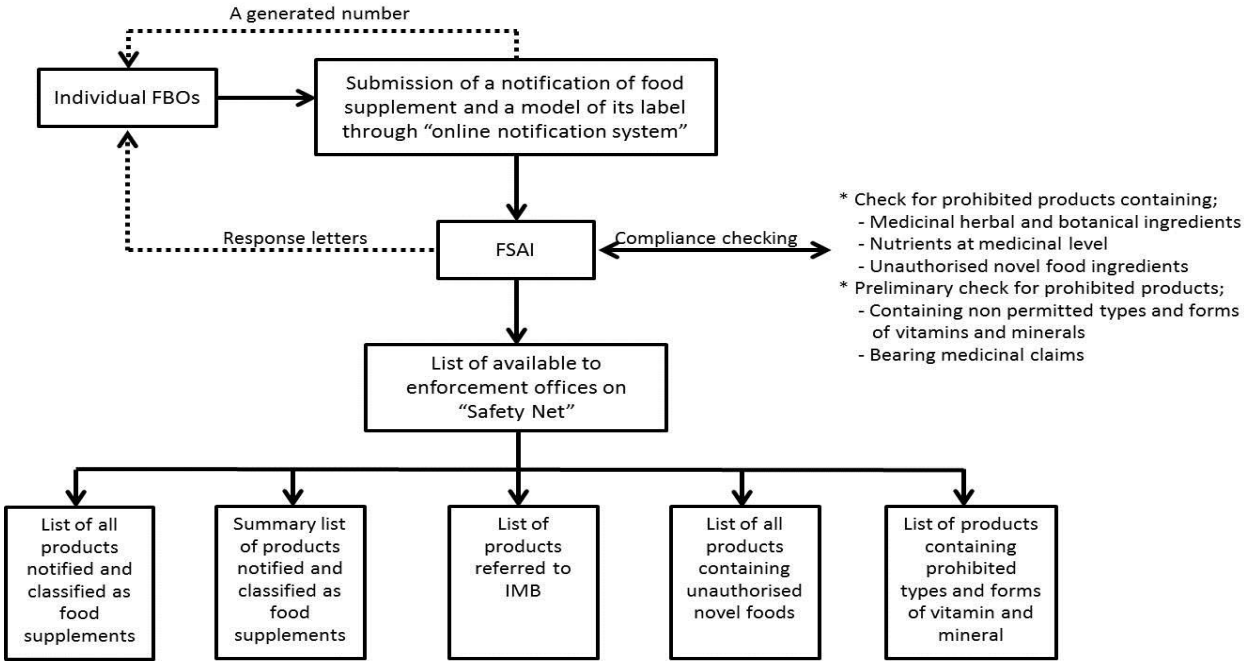


Figure 10 Summary of FSAI process for assessing notified food supplements (FSAI, 2010e)[101]

Since setting of the maximum and minimal levels of micronutrients used in supplements is still in process, the on-line Irish food composition database for nutrients has been developed by collecting data on food specific to the Irish population including manufactured products, composite dishes, and nutritional supplements between 1997 and 2006. The nutritional supplements comprised 10% of this database and served an important source to explore the impact of micronutrient supplement intakes and to evaluate the risk of supplement users exceeding the UL (Black et al., 2011).

2) Premises Perspective

Apart from the EC directive 2002/46/EC, the provisions of food supplement are complied with other related regulations and requirements of Community level (FSAI, 2010d). General requirements based on the GFL are fully implemented in supplements placed on the Irish market such as traceability system requiring "one step back- one step forward" approach. Minimal information shall be recorded in all cases and to be made available on demand are:

1. Name and address of supplier and name of product which were supplied to the food business operator by the supplier;

2. Name and address of business customer and name of products that were delivered by the food business operator to that customer; and

[101] FSAI, 2010, modified from p.22

3. Date of transaction/delivery

Establishments of food supplements shall be legally registered and complied with Regulation (EC) 852/2004 on the hygiene of foodstuff, and recommended best practices should be involved in the production operation as appropriately decided by the FBOs. Types of quality management systems applied in chain of food supplements may vary from the FBO to another or from each step of the chain like GMP, ISO 9000, or ISO 22000 depended on the discretion of the Environmental health officers (EHOs) responsible to carry out the inspection of food supplement establishments. In case of no GMP system in place, the manufacturer is responsible to provide sufficient evidence to the inspectors to ensure that the critical steps of production have been taken into account on safety and consistency of the supplements as well as legal compliance. In addition, in case of any major change of the production resulting in impact of product safety, e.g., changes new premises, change product formulation, change test method or change material specifications, the FBOs should provide credible documents to the EHOs to guarantee that there is no impact on product safety and quality to consumer health (FSAI, 2012a).

3) Presentation Perspective

Requirements on presentation, labelling, and advertising supplements entirely comply with related EC directives. In Ireland, once a registering authority grants a FBO approval, a certificate of approval will be issued. This certificate contains following information:

1. The name of the holder of the food business approval;

2. The address of the premises to which the food business approval relates,

3. The nature of the activity to which the approval relates;

4. The conditions to which the approval is subject;

5. The period of validity (if any) of the approval; and

6. A unique reference number that identifies the food business.

The certificate of the presentation shall be prominently displayed on the premises during business hours.

In principle, the labelling, presentation, and advertising of food supplements must not attribute product the property of preventing, treating or curing a human disease, or refer to such properties[102]. They also shall not include any mention stating or implying that a balanced and varied diet cannot provide appropriate quantities of nutrients in general[103]. Nutrition and health claims shall be complied with Regulation (EC) No. 1924/2006, especially in health claims clarified to Article 13(5) and Article 14 that shall be submitted to the FSAI for evaluation by the EFSA, while the procedures and required documents are available on the FSAI websites (FSAI, 2009a) (FSAI, 2012b). The FSAI provides the list of approved and rejected health claims under Article 13(5) and 14 available on the website for easy accessibility and transparency (FSAI, 2012g). In addition, a list of permitted and non-authorised Art 13 claims containing of 222 permitted health claims has been established under Commission Regulation (EU) No. 432/2012. From

[102] Regulation 5(3) of the S.I No. 506 of 2007
[103] Regulation 5(5) of the S.I No. 506 of 2007

the point of view, the Irish food supplements requirements regarding packaging, labelling, and presentation can be summarised as follows (Cox, 2010):

Table 6 Summary of Irish requirements related to presenting food supplements

Criteria	Requirement
Source/origin	The place of origin must be stated to prevent consumers from misleading
Name	The product must: - be sold under the name "Food supplement"; - state the product name with a product description; - state the name or business name and address of the manufacturer or packager or seller within the EU
Ingredients	The label shall include: - the list of ingredient; - the quantity of each ingredient; - the amount of the nutrients/substances with a nutritional or physiological effect in numerical form and the amount should be per portion of the product as recommended for daily consumption; -information on vitamins and minerals as a percentage of the reference values
Amount of the product	The net quantity should be addressed
Compulsory information, warning or statements	The label must contain following information: - the names of the categories of nutrients or substances that characterise the product or an indication of their nature; - the portion of the product recommended for daily consumption; - a warning not to exceed the stated recommended daily dose; - a statement to the effect that food supplements should not be used as a substitute for a varied diet; - a statement to the effect that the product should be stored out of the reach of young children; - The date of minimum durability; and - Storage instruction
Language	Food sold in Ireland must be labelled in English, or in Irish and English. Other languages may be labelled but only in addition to English.
General features of a label	The information provided on the label must be easy to understand and be clearly legible. It must also be indelible, easy to see and not obscured in any way.
Other remarks	There is no prescribed font or text size for the labels

To assist the legal requirements on advertisements, the ASAI, an independent self-regulatory body set up and financially supported by the advertising industries, also sets up codes of standards for advertising food supplements including enforcement and cooperating activities among advertisers, agencies

and media. The main objective is to ensure that all commercial marketing communications are legal, decent, honest and truthful. The standards of advertising vitamins, minerals and food supplements are addressed in Article 8.14 – 8.16 of Health and Beauty section (ASAI, 2010) which can be summarised as follows:

1. Advertisers may offer supplements as a safeguard and may refer to the micronutrient content of a particular product, but should not suggest that there is a widespread vitamin or mineral deficiency. Marketing communication should not imply that supplements will guard against dietary deficiency or enhance performance as well as promote as a substitute for a healthy diet. The communication should not claim that the supplement is capable of preventing, treating, or curing disease.

2. Marketing communications may advertise micronutrient supplements to certain categories of people, e.g. elderly, children, and athletes in training.

3. Marketing communications should not suggest that the replacement of supplement will influence the speed or extent of illness recovery while the prescription in such cases for a doctor and self-medication should not be encouraged.

3.2.1.5 PROBLEMS AND CHALLENGES IN REGULATIONS AND PRE-MARKET CONTROL SYSTEM

Even many requirements are asked from the FBOs to produce and control safety and efficacy of food supplements before placing on the market, many problems challenging competent authorities to deal with. Confusion on classification and interpretation of a multitude of products contained micronutrients available in the market is still an issue for consumers. For example, powders packed in containers marketed to enhance performance are classified as food supplements as well as a performance enhancing drinks if presented as a "concentrated source" and sold in dose form. On the other hand, other performance drinks which are sold in a normal form and are therefore not considered as a food supplement despite the energy claims which may be made. If these products have unclear statement on the label, consumers may not be able to distinguish these different categories resulting in misleading and overdose consumption. Micronutrients are often added in various food, supplements, and medicinal products such as folic acid which could be used in food as a functional food as well as it is safely certified as medicinal product (Petroczi et al., 2011). It has been obviously noted that micronutrients can supplement to either food, supplements, or medicinal product, but purpose of usage and declaration on their labels is a critical point to clarify the product categories.

The risk of harm occurring from taking supplements will depend on the safe intake range of the nutrient concerned. Too much intake micronutrients exceeding than the maximum level may result in health risk due to the high toxicity, however too low consumption may cause deficiency of essential nutrients for health. Moreover, the width of this range is highly variable depending on type of nutrients such as the water-soluble vitamins (e.g. vitamin C) have a greater margin of safe intake set at $\geq$ 1 g which is 10-fold difference from the reference intake, while the recommended intake of vitamin A (one of fat-soluble vitamins) is 600-900 µg retinal equivalents (RE) per day and scientific evidences for adverse effects on bone health at intake > 1,500 µ RE per day or only < 2-fold higher (Mulholland & Benford, 2007). To prevent consumers from an inappropriate intake level of multi-micronutrients, the positive list of permitted vitamins and minerals in food supplements has been established on the risk assessment basis (Eberhardie, 2007), however, the list does not recognise all existing micronutrients applied in the products as well as maximum level of these substances still be discussed among stakeholders which is a big challenge for the EC

to make an applicable decision. Furthermore, the positive list and pre-authorisation of a new substance may limit production development and application of new technology for food supplements. Since the maximum levels of vitamins and minerals are based on a nutrient-appropriate risk assessment methodology resulting in different levels of each country while no limits are established in law and the manufacturer is required to ensure products brought to market are safe. Therefore, the harmonised same maximum level of micronutrient supplements is much difficult but the shift forward a safety-based approach is recommended to apply in the supplements (Pettman, 2011).

One of problems concerned on food supplements is about health claims, especially in pre-approval process regarding Article 13.5 and 14 of the Regulation (EC) 1924/2006. By October 2009, EFSA had received a total of 282 dossiers submission which are 213 claims concerning on children, 47 relating to disease reduction claims, and 22 concerning on new scientific evidences but almost 80% of which were rejected (Buttriss & Benelam, 2010). Main reasons of this failure are such as 1) insufficient evidence showing cause and effect relationship between the consumption of the food or constituents and the claimed effect; 2) the existing evidence is inconclusive, and 3) a cause and effect of the relationship has not been established (Verhagen et al., 2010). Even the claims are received positive opinions from EFSA and undergoing the authorisation procedure, key challenges are not only how to combine the wording of claim which reflects scientific proof with wording which consumers can understand easily, but also how to translate the approved claims to different MS languages with the significantly similar meaning (Gilsenan, 2011).

3.2.2 US: Federal and State systems

The DSHEA of 1994 is a principal regulation applied for dietary supplements in US collaborating with other relevant regulations such as the FD&C Act of 1938 and the NLEA of 1990 for comprehensively controlling safety of these products.

3.2.2.1 REQUIREMENTS OF PRODUCT PERSPECTIVES

Under the DSHEA of 1994, FBOs are neither legally required to register their product nor received approval from the U.S FDA before producing or selling dietary supplements. They are obligated by law to report the U.S. FDA only the serious adverse events regarding the products, but mild and middle adverse reports are on voluntary basis (Brownie, 2005). Unlike the EU directive, there is no any positive list provided for permitted ingredients because the DSHEA was proposed as an industry-friendly basis and approved by the US Congress in a principle concept that the supplements are safe within a broad range of intake while consumer should be able to make choices about preventive health care programmes based on scientific evidences related to the supplements (S. A. Mason, 2010). However, the FBOs must ensure that the product are safe sufficiently supported by scientific data and the information on product label is not misleading to consumers.

1) Old and new substances

For safety requirements of both old and new substances of dietary supplements, the scientific evidence are equally needed to ensure the safety of product based on DSHEA, but the burden of proof and the presumption are reversed (Hatchcock, 2001). In case of an old ingredient or called “grandfathered ingredient” which is marketed before October, 15 1994, it shall not be required pre-market authorisation

by the U.S. FDA but it must not be adulterated. The U.S. FDA shall bear the burden of proof if the dietary supplement or its ingredient falls into following elements[104]:

1. Present a significant or unreasonable risk of illness or injury under: (i) conditions of use recommended or suggested in labelling or; (ii) if no condition of use are suggested or recommended in the labelling, under ordinary conditions of use;

2. Be declared by the U.S FDA to pose an imminent hazard to public health or safety;

3. Contain a dietary ingredient that renders it adulterated under the condition of use recommended or suggested in the labelling of such dietary supplement.

When there is significantly scientific evident to proof that the dietary supplement is adulterated, the Secretary of HHS shall report to the US attorney for a civil proceeding and the US Court for further decision making.

On the other hand, a new ingredient referring to a substance which is first marketed after October, 15 1994 may concern as unsafe and the dietary supplement containing this new substance shall be adulterated, unless it meets one of these following requirements[105]:

1. The new ingredient has been presented in the food supply as an article used for food in a form in which the food has not been chemically altered; or

2. There is a history of use or other evidence of safety establishing that under recommended or usual conditions its can reasonably be expected to be safe.

Since there is no authoritative list of dietary ingredients that were marketed in dietary supplements before October 15, 1994, FBOs are responsible for determining if an ingredient is a "new dietary ingredient" and, if not, for documenting that a dietary supplement that contained the dietary ingredient was marketed before October 15, 1994. Therefore, if it is obviously clarified as a “new ingredient”, the FBOs shall be responsible for pre-market process by notifying the new ingredient with relevant scientific evidences to the U.S. FDA at least 75 days before the product being placed on the market. In line with requirements for pre-market notification[106], the original and two (2) copies of the notification and following information shall be provided (U. S. FDA, 2012b):

1. Name of applicant and completed address;

2. Name of the new dietary ingredient with a description of the dietary supplement or dietary supplements that contain the new dietary ingredient, including:

- Level of the new dietary ingredient in the product;
- Conditions of use of the product stated in the labelling or the ordinary conditions of use;

[104] Section 402 (f) of the FD&C Act amended by Section 4 of the DSHEA
[105] Section 413 (a) of the FD&C Act
[106] 21 CFR §190.6.

- History of use or other evidence of safety establishing that the dietary ingredient, when used under the conditions recommended or suggested in the labelling of the supplement, will be reasonably expected to be safe;
- Any reference to published materials must be accompanied by reprints or photostatic copies;
- Any material in a foreign language must be accompanied by a translation.

3. A signature by a person designated by you who can be contacted if we have questions.

After receiving the pre-market notification, the U.S. FDA will acknowledge its receipt in writing to the FBOs within 75 days including the date of receipt which is a the filing date. For 75 days after the filing date, the product cannot be placed on the market and the FBO may be requested to provide additional information with regard to the new ingredient. These data will be kept in a confidential condition for 90 days following its receipt, and then this information shall be placed on public display which is available on the U.S. FDA website[107], except matters in the information which are trade secret or commercial information[108]. It notes that this public list of new ingredients does not establish a finding by FDA that a new dietary ingredient or a dietary supplement that contains a new dietary ingredient is safe or is not adulterated[109]. It also does not mean that another manufacturer can lawfully market the dietary ingredient in a dietary supplement; therefore each manufacturer is responsible for ensuring compliance with the Act (U. S. FDA, 2012b).

2) Maximum safe level of vitamins and minerals

There is neither maximum safe level of ingredients in dietary supplements nor rules that limit a serving size or the amount of a nutrient in any form of the supplements. This decision is made by the manufacturer and does not require the U.S. FDA to review or approve (U. S. FDA, 2012b). However, based on the latest report of the National Academy of Science and Committee on Dietary Allowance, it suggests consumers to adequately consume micronutrients complied with the recommended daily allowance (RDA) which is based on needs of the average person. Intake vitamins in amounts 10 times higher than the RDA may be harmful, therefore, amount of micronutrient consumption should not exceed the RDA, unless recommended by the medicinal professionals (Jiang & Zhang, 2009).

3) Other safety requirements for product perspective

Since a dietary supplement is classified as a food product, other safety requirements for the supplement are as same as apply in conventional foods (Hatchcock, 2001). Food is deemed to be adulterated if it contains any poisonous or harmful substance to consumer health and the U.S. FDA has to oversee the safety of food product along the supply chain by monitoring programmes as well as risk assessment of potential exposure such as national toxins, pesticides, and other chemical contaminants, for examples, dioxins, acrylamide, and lead[110]. Moreover, new food additives shall be pre-approved by the U.S. FDA, unless they are classified as GRAS ingredients. The GRAS status may be achieved in the

[107] In docket number 95S-0316 at FDA's Dockets Management Branch, http://www.fda.gov/RegulatoryInformation/Dockets/default.htm
[108] Section 8 of the DSHEA of 1994
[109] Section 21 of the U.S.C. 342
[110] Section 402 (a)(1) of the FD&C Act

following three ways (Hatchcock, 2001): 1) a history of use; 2) self-declaration by the manufacturer; and 3) confirmation by the U.S. FDA.

A food-contact substance defines to any substance intended for use as a component of materials used in manufacturing, packing, packaging, transporting, or holding food if such use is not intended to have a technical effect in such food is also controlled under the amended FD&C Act (U. S. FDA, 2011b). Similar to food additives, a new food contact substance shall be pre-notified to the U.S FDA with scientific evidences ensuring on safety such as chemical identity, manufacturing process, physical properties and specifications, condition of use, intended technical effect, and stability data.

3.2.2.2 REQUIREMENTS OF PREMISES PERSPECTIVES

In general, FBOs are required to register their domestic and foreign facilities that manufacture, process, pack, or hold food for human or animal consumption in the US with the U.S. FDA by December 12, 2003 before producing or selling food products[111]. Moreover, after the FDA Food Safety Modernization Act (FSMA) signed into law on January, 4, 2011, it amended section 415 of the FD&C Act[112] which requires all food facilities to renew their registrations with the U.S. FDA during the period beginning on October 1 and ending on December 31 of each even-numbered year (U. S. FDA, 2012d). For dietary supplements, the registration of facilities is also required like other food products, but a set of GMP standard shall be specifically established and the expiration date on the product label shall be required[113]. In 2007, the U.S. FDA published a final rule of current GMP (CGMPs) in manufacturing, packaging, labelling, or holding operations for dietary supplements (GPO, 2007). This rule consists of 16 subparts with new subparts focusing on specific aspects of manufacturing process or addressing specific issues resulting in user-friendly to ensure the consistent quality of the dietary supplements. All domestic and foreign companies that manufacture, package, label, or hold these products, including those involved with the activities of testing, quality control, packaging, labelling, and distributing them in the US shall comply with the CGMPs rule which enters into force August 24, 2007 but it is fully effective in June, 2008 for large companies while small business have three-year phase for fully compliance. From the rules, manufactures are required to:

1. Employ qualified employees and supervisors;

2. Design and construct their physical plant in a manner to protect dietary ingredients and dietary supplements from becoming adulterated during manufacturing, packaging, labelling and holding;

3. Use equipment and utensils that are of appropriate design, construction, and workmanship for the intended use;

4. Establish and use master manufacturing and batch production records;

5. Establish procedures for quality control operations;

[111] The Public Health Security and Bioterrorism Preparedness and Response Act of 2002
[112] 21 U.S.C. § 350d
[113] Section 402, 21 U.S.C. 342

6. Hold and distribute dietary supplements and materials used to manufacture dietary supplements under appropriate conditions of temperature, humidity, light, and sanitation so that the quality of the dietary supplement is not affected;

7. Keep a written record of each product complaint related to CGMPs; and

8. Retain records for 1 year past the shelf life date, if shelf life dating is used, or 2 years beyond the date of distribution of the last batch of dietary supplements associated with those records.

In addition, there is the interim rule issued by the U.S. FDA to allow manufactures for exemption from the requirement of full identity testing of one or more dietary ingredients used. The manufacturer should provide sufficient data to show that its proposed reduced frequency of identity testing dose not substantially reduce assurance that the ingredient is correctly used. The U.S. FDA will consider each petition on a case-by-case basis.

3.2.2.3 REQUIREMENTS OF PRESENTATION PERSPECTIVES

After enforcing the DSHEA, dietary supplements must be labelled a "dietary supplement" including other particular criteria in order to distinguish from conventional or fortified foods. Under section 5 of the DSHEA, a publication including an article, a chapter in a book, or an official abstract of a peer-reviewed scientific publication used as supporting information of supplement shall not be defined as labelling and shall not be misleading to consumers. It must neither promote a particular manufacturer or brand of a dietary supplement nor add on the product by sticker including any other method. The provision highlights that these supporting information shall not be false or misleading to consumers and a task of burden of proof shall be bound by the U.S FDA[114].

1) Labelling

The specific requirements of labelling on supplement ingredients and nutrition information stipulates in Section 7 of the DSHEA are as follows (U. S. FDA, 2005):

1. The statement of identity (name of the dietary supplement);

2. Net quantity of contents statement (amount of the dietary supplement);

3. Supplement facts specifically applied in the dietary supplements instead of nutrition label in conventional foods;

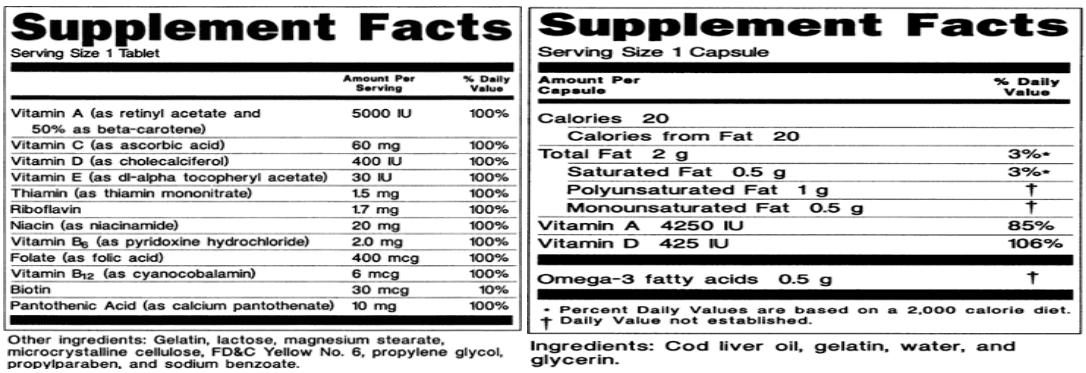
4. List of ingredients; and

5. Name and place of business of the manufacturer, packer, or distributor.

Information in above item 1 and 2 shall be addressed in the principal display panel whereas other items must be displayed in the information panel. This information shall be obviously prominent, conspicuous, and easy-to-read on the product label. The U.S. FDA describes that the front size must be at least one-sixteenth (1/16) inch in height based on the lower case letter "o," and not be more than three times as high

[114] Section 403 B (c)

as they are wide. The lettering must contrast sufficiently with the background so as to read easily. For supplement facts, specific names and quantities of dietary ingredients based on serving size and/or serving per container shall be listed. Apart from primary information needed to be present on the supplement facts such as total calories, calories from fat, total carbohydrate, sugar, and protein, all micronutrients intentionally added for supplementation must be contained in the supplement fact. In case of insufficient information of daily values, dietary ingredients shall be listed by their common or usual names with using a symbol in the column of "% Daily Value" referring at the footnote to "Daily Value Not Established". Examples of supplement fact are as below:



Supplement Facts

Serving Size 1 Tablet

	Amount Per Serving	% Daily Value
Vitamin A (as retinyl acetate and 50% as beta-carotene)	5000 IU	100%
Vitamin C (as ascorbic acid)	60 mg	100%
Vitamin D (as cholecalciferol)	400 IU	100%
Vitamin E (as dl-alpha tocopheryl acetate)	30 IU	100%
Thiamin (as thiamin mononitrate)	1.5 mg	100%
Riboflavin	1.7 mg	100%
Niacin (as niacinamide)	20 mg	100%
Vitamin B_6 (as pyridoxine hydrochloride)	2.0 mg	100%
Folate (as folic acid)	400 mcg	100%
Vitamin B_{12} (as cyanocobalamin)	6 mcg	100%
Biotin	30 mcg	10%
Pantothenic Acid (as calcium pantothenate)	10 mg	100%

Other ingredients: Gelatin, lactose, magnesium stearate, microcrystalline cellulose, FD&C Yellow No. 6, propylene glycol, propylparaben, and sodium benzoate.

Supplement Facts

Serving Size 1 Capsule

Amount Per Capsule	% Daily Value
Calories 20	
Calories from Fat 20	
Total Fat 2 g	3%*
Saturated Fat 0.5 g	3%*
Polyunsaturated Fat 1 g	†
Monounsaturated Fat 0.5 g	†
Vitamin A 4250 IU	85%
Vitamin D 425 IU	106%
Omega-3 fatty acids 0.5 g	†

* Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

Ingredients: Cod liver oil, gelatin, water, and glycerin.

(A) (B)

Figure 11 Sample labels of Dietary supplement containing multiple vitamins (A), and with- and without % daily value (B) (U. S. FDA, 2005)

However, the supplement fact may exclude from the product label if there is insignificant amount of nutrients, limitation of annual sale (less than $500,000 in total annual sales), or its package is too small to bear nutritional information (Greene, Prior, & Frier, 2001).

2) Claims

On the legal basis, there are three types of claims permitted for dietary supplements (U. S. FDA, 2005):

1. Nutrient content claims (NNC) mean any claim expressly characterizes the level of a nutrient in a dietary supplement. Terms using for nutrient content claims are such as free, high, and low, or they compare the level of a nutrient in a food to that of another food, using terms such as more, reduced, and light. The permitted NNC has been specified in the section 21 CFR 101, Subpart D (Specific Requirements of Nutrient Content Claims), therefore, NNCs other than the permission list shall not be allowed to declare on supplement label. Specific requirements for NNC are as follows:

- Front sizes of the claim may be no larger than twice the type size of the statement of identity (the name of the food) and may not be excessively prominent in style compared to the statement of identity;

- A panel of Supplement fact;

- A disclosure statement, in case that a dietary supplement contains one or more of the following nutrients in excess of the levels listed below per reference amount customarily consumed, or per labelled serving; Fat 13.0 grams, Saturated Fat 4.0 grams, Cholesterol 60 milligrams, Sodium 480 milligrams. Front

sizes of the disclosure statement are required as the same as those for the net quantity of contents statement[115], except where the size of the claim is less than two times the required size of the net quantity of contents statement, in which case the disclosure statement is no less than one-half (1/2) the size of the claim, but no smaller than one-sixteenth (1/16) of an inch. A disclaimer statement of one thirty-second (1/32) of an inch is allowed if a product package has less than three square inches of available label space and is an individual serving-size package served with meals in restaurants.

2. Structure/function claims refer to any statement claims related to roles of a nutrient or dietary ingredient intended to affect structure or function in humans, or to maintain such structure or function. It also includes any claim describes the general well-being from consumption of the dietary ingredients or benefit related to a classical nutrient deficiency disease[116]. FBOs who would like to use this kind of claim shall provide substantiation to ensure the claim is truthful and not misleading to consumers. Although this claims is not required the pre-approval from the U.S. FDA, FBOs must notify this claim within 30 days after the first marketing of the supplement by sending an original and two copies of the notification to the U.S. FDA. Another legal requirement is to provide the disclaimer statement by using the following an unique sentence, as appropriate[117]:

- Singular: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease;" or

- Plural: "These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease."

The text size of the disclaimer must be in boldface type which is not smaller than one-sixteenth (1/16) inch. To notify the claim, following information is included:

- The name and address of the manufacturer, packer, or distributor of the dietary supplement that bears the statement;

- The text of the statement;

- The name of the dietary ingredient or supplement that is the subject of the statement; and

- The name of the dietary supplement (including its brand name) on whose label, or in whose labelling, the statement appears.

3. Health claims imply to any statement describes a relationship between an ingredient and a disease or a health-related condition, e.g. “calcium may reduce the risk of osteoporosis”. They are basically required evaluation and authorisation from the U.S. FDA before placing on the label. A list of authorised health claims is provided in Appendix C the “A Dietary Supplement Labelling Guide” and also available on the FDA website[118]. Moreover, The U.S FDA has published a qualified health claim in Appendix F of the guidance. The qualified health claim is supported by less scientific proof than an authorised health claim and shall be specified a disclaimer statement to explain the level of the scientific evidence supporting the

[115] 21 CFR 101.105(i)
[116] Section 101.93(f) of the FD&C Act
[117] Section 403 (r)(6) of the FD&C Act
[118] Link of the information: A Food Labelling Guide-Appendix C.

claim, unlike the authorised health claim. Any new health claim including new disclaimer shall be submitted to the U.S. FDA for approval and may be legally used after the U.S. FDA issues by either an authorisation regulation or a letter stating enforcement discretion conditions for the qualified health claim.

Table 7 Examples of authorised health claim and qualified health claim (U. S. FDA, 2005)

Type	Example of claim	Specific requirements
Authorised health claim	***Calcium, vitamin D and osteoporosis:*** Adequate calcium and vitamin D, as part of a well-balanced diet, along with physical activity, may reduce the risk of osteoporosis.	- For calcium, vitamin D and osteoporosis claim-high in calcium and vitamin D - Supplements must disintegrate and dissolve, and Phosphorus content cannot exceed calcium content
Qualified health claim	***B Vitamins & Vascular Disease:*** As part of a well-balanced diet that is low in saturated fat and cholesterol, Folic Acid, Vitamin B6 and Vitamin B12 may reduce the risk of vascular disease.	- For dietary supplements containing vitamin B6, B12, and/or folic acid - The disclaimer shall be addressed below the claim as "FDA evaluated the above claim and found that, while it is known that diets low in saturated fat and cholesterol reduce the risk of heart disease and other vascular diseases, the evidence in support of the above claim is inconclusive"

3) Advertisements

Regulations regarding advertising dietary supplements throughout print, broadcast advertisement, websites, catalogues, and similar direct marketing materials are enacted by the FTC working close collaboration with the U.S. FDA. The FTC's work is direct by different laws resulting in different procedures on product claims. For example, unproven health claims on labelling are expressly prohibited by the U.S FDA while such claims in advertisements are not lawfully required for permission from the FTC (Yeung et al., 2006). The FTC's substantiation standard is flexible depending on several factors; however, its justification shall ensure that the advertising dietary supplements must be truthful, not misleading, and scientifically substantiated. To comply with relevant requirement of advertising dietary supplements, "An Advertising Guide for Industry" (FTC, 2001) published since 2001 describes two-step process of advertising interpretation and substantiation apply in the context of supplement including relevant issues as follows:

Step 1: Identification and interpretation of advertisement meaning. To draft an advertising claim, accuracy of claims suggested or implied by the advertisement is critically concerned. All elements consisting of the advertisement including text, product name, pictures shall be entirely assessed as "net impression" in order that consumers are able to understand the advertising claim correctly. Evidences on consumer interpretation can be valuable but it is not necessary. In case of advertising claim that makes either an express or implied safety representation should include information about any significant safety risk or warning statement to public consumers such as an advertisement for a multi-vitamin/mineral supplement claim that "the product can eliminate a specific deficiency resulting in feeling of fatigue. In fact, less than 2% of the general population to which the advertisement is targeted suffers from this deficiency". The Advertiser should disclose this fact so that consumer

will understand that only the small percentage of people who suffer from the actual deficiency are likely to experience any reduction in fatigue from using this product[119]. If the qualifying information is needed for disclosure, it should be obviously presented to consumers, e.g. clear language, big front type, placing close to the claim.

Step 2: Substantiation of advertising claims. The FTC's standard for evaluating substantiation is sufficiently flexible depending on relevant factors with the claim such as

- Type of product. If a product is related to consumer health on safety, the substantiation is highly required.

- Type of claims. If the claim is difficult for consumer to access on their own understanding, a more exacting standard of evaluation will be applied.

- The benefit of a truthful claim and the cost/feasibility of developing substantiation for the claims. Both factors are equally considers for appropriate benefits to consumers and FBOs.

- The consequences of a false claims and amount of substantiation that experts in the field believe.

In general, numbers or types of substantiation including scientific research are not specified but consideration on quality and adequate information to support the specific advertising claim are more important. Moreover, all relevant researches relating both benefit and adverse effect of the supplement shall be equally considered before making an advertising claim to avoid any claim which is likely unsubstantiated and misleading. For example, an advertiser wishes to make the claim that a supplement will substantially reduce body fat, however, based on the scientific study, no statically significant difference between test and control groups. Given the totality of the scientific evidence on this subject, the claim is likely to be unproven[120]. The advertiser shall keep in mind that any advertising claim should not be exaggerated context, nature, or performance of the effect achieved in a study and should not suggest greater scientific certainty than actually exists.

Other issues of advertising dietary supplements, particularly in micronutrients are:

- Although the DSHEA of 1994 does not apply to advertising, there are situations where such a disclaimer required from the product claims is desirable in advertising as well as in labelling to prevent consumers from being misled about the nature of the product and the extent to which its efficacy and safety have been reviewed by regulatory authorities. Compliance with the notification and disclaimer provisions of the DSHEA does not constitute authorisation of a claim by the U.S. FDA and advertisers should not imply that the U.S. FDA has specifically approved any claim on that basis.

- Claims based on consumer testimonials, or expert endorsement could not be directly accepted and other scientific information is needed to back up the advertising claims. Substantiation related to Individual consumer experiences or expert opinion is insufficient information to support any advertising claims, comparing to evidences from whole consumer perceptions, or a group of experts.

[119] Example 5, an Advertising Guide for Industry.
[120] Example 19, an Advertising Guide for Industry.

- Substantiation based on third party literatures e.g. newspaper articles, abstracts of scientific studies shall be conscious. The FTC will justify this information based on scientific sound and they shall not mislead to consumers.

3.2.2.4 SPECIFIC REQUIREMENTS AT STATE LEVEL (NEW YORK CASE STUDY)

According to the chapter 2, the federal law is the supreme regulation of the land; however the U.S. Congress often set a federal minimal requirements regarding health and safety laws intending to leave opportunity for additional state regulations. The report of New York State Task Force on Life & Law (Law, 2005) addressed that regulations on drug and food including dietary supplements have been largely issued at federal level and several states have passed these laws into state requirements. For dietary supplements, various federal regulations are applied to supplement industries at the state levels such as labelling & marketing requirements and restriction on sale and distribution. Under the DSHEA of 1994, nutrition content and labelling rules are not different between the federal and state level but warning statements can be additionally provided by the state law. For micronutrients, the federal requirements regarding product, premises, and presentation aspects directly enforce into state level such as the New York State which is selected for a case study based on information accessibility.

The New York State Department of Health (DOH) and the New York Statement of Agriculture & Markets (DAM) play an important role in responsibilities of food regulations. The DAM generally controls manufacture and sale of packaged food while the DOH focuses on food prepared and consumed on-site e.g. in restaurants. However, the DOH and DAM neither conduct testing for adulteration or contamination of supplements, nor inspect establishments of dietary supplements. Most dietary supplement businesses located in this state are voluntarily registered with the DOS; therefore the state has no means of identifying all supplement industries located in the state. In case of emergency problem on dietary supplements, the DOH has capability to test the products at the State, as necessary. Apart from two main agencies, there are two more agencies working to support regulations and safety requirements on the supplements. The State Attorney General acts against false or misleading business practices by the States' Consumer Protection Act. If this agency receives any serious supplement-related complains, they will be forward to both the DOH and the U.S. FDA. Another agency is the Office of Regulatory Reform (ORR) under the DOH has tasks to support the regulatory reform agenda as well as to facilitate a more efficient and user-friendly rules of dietary supplements.

According to the New York case study, neither specific nor additional requirements are enacted at the state level. Main reasons may be related to no pre-market requirements for dietary supplements in US while burden of proof and notification of product labelling including claims are conducted by the U.S. FDA. Advertisements and product presentations via other public channels are also controlled under federal rules by the FTC. Agencies at a state level, therefore, work only to collaborate with central agencies and support the enforcement of relevant regulations based on the federal rules.

3.2.2.5 PROBLEMS AND CHALLENGES IN REGULATIONS AND PRE-MARKET CONTROL SYSTEM

Confusion on product classification still issues from consumers since the U.S. FDA does not technically define terms of functional foods and neutraceutical products that may mislead to consumers. By enforcing the DSHEA of 1994, FBOs are not legally required to notify or get approval from the U.S FDA before placing their products on the market resulting in the increase in product development, availability of new supplements for consumer choice, while unsafe products cannot be immediately withdrawn or recalled if the

U.S. FDA cannot prove that they has violated the regulations related to safety, information, labelling or claims at significant or unreasonable risk to the consumer (Brownie, 2005). The process of burden of proof is laborious and time-consuming that leads to delay response on preventative measures, an example of the removal of ephedra alkaloids came about ten years after the U.S. FDA issued its initial advisory against it in 2003 (S. A. Mason, 2010). Moreover, there is neither permitted list nor safe levels of micronutrients applied in supplements provided to the FBOs for legal compliance as well as to the competent authorities for post-market monitoring. Therefore, the U.S. FDA still has huge obstacles to protect consumer due to limitation of information relating to identity and ingredients of supplements available in the market, the number and location of dietary supplement firms, and number of adverse effect reports (S. A. Mason, 2010). Even new ingredients shall be notified to the U.S. FDA within 75 days prior to be present in the dietary supplements, this provision does not guarantee that the substance is safe for consumption. FBOs also misunderstand or ignore this notification, while scientific evidences submitted to the U.S. FDA were mostly inadequate safety data (Gershwin et al., 2010). On the other hand, old ingredients do not require any scientific supports from the FBOs that may make significant risk to the consumers. For premises, the CGMSs rule required manufacturers to establish specification for identity, purity, quality, and necessary control measure of the product, however the validated analytical standards and methods were not yet established (FTC, 2001).

For the presentation perspective, the DSHEA of 1994 provides some safeguard measures to protect consumers by requiring a disclaimer statement for structure/functional claims as well as pre-market authorisation of health claims in relation to dietary ingredients, though, these requirements do not comprehensively implement for the product advertisement including internet and direct sale channels. For advertising dietary supplements, several FTC cases challenged misleading advertisement that referred to scientific studies as proving the product's efficacy, when in fact for various methodological reasons the studies did not support the specific claims made in the advertisement (Gibson & Taylor, 2005). Inconsistency of information concerning on products' health benefit is also one of difficulties for consumers to make a choice correctly.

Public perception on dietary supplement and its regulations is mostly different from the reality. The survey result of consumer perception (Gershwin et al., 2010) showed that almost 60% of respondents believed the dietary supplements must be approved by competent authorities like the U.S. FDA before placed on the market.

3.2.3 Thailand

The notification of the MoPH, No. 293 B.E. 2548 (2005), Re: Food Supplement or called "the Notification No. 293" (T. FDA, 2005) is a principal regulation enforcing and controlling dietary supplements in Thailand. It notified as of 15 December, 2005 and come into force 90 days after published in the Government Gazette[121]. Other relevant requirements are also addressed in this notification such as premises and product registrations, label approval, nutritional labelling, nutrient contents and claims, safety issues on pathogens, food additives, and packaging. Under clause 4 of the Notification No. 293, dietary supplements are classified as the food subject to the qualities and standards and label shall be approved

[121] Vol. 122, Special Part 150 Ngor, dated 28th December, 2005

before use. Therefore, all of supplements sold in Thailand shall comply with registration procedures and safety requirements issued by the Thai FDA.

3.2.3.1 REQUIREMENTS OF PRODUCT PERSPECTIVES

1) The positive List and new substances

Dietary supplements containing permitted micronutrients shall be registered by the Thai FDA before placing them on the market or exporting to other countries. The positive list of the permitted vitamins (13 types) and minerals (14 types) including amino acids was approved by the Food Committee[122], and notified in the Announcements of the Thai FDA on June 1st, 2006 (T. FDA, 2006b). The list consists of type and form of each micronutrient, e.g. Vitamin A and other forms like retinol, retinyl acetate, retinyl palmitate, or beta-carotene. According this positive list, the maximum limit of each micronutrient contained either single or multi forms shall not exceed the Thai RDI. A procedure of pre-registration for dietary supplements consisting of permitted micronutrients is summarised as the below procedure (T. FDA, 2007):

Step 1: Document preparation. These following scientific evidences shall be prepared by the FBOs;

For domestic market	For exporting market
1. Copy of manufacturing License; or Production License (for small business); or Import Food into the Kingdom License (in case of imported dietary supplement)	1. Copy of manufacturing License or Production License (for small business)
2. Certification of manufacturing premises* (in cased of importation)	2. Document from a buyer to demonstrate that the product is allowed to place on the importing market.
3. Formula and detail of each ingredient present by unit or weight in percentage	3. Formula and detail of each ingredient present by unit or weight in percentage
4. Raw material specification	4. Specification and quality of product
5. Specification and detail of packaging, dose of consumption, instruction of use, instruction of storage, and expiration date	

Remark: * it shall be complied with announcement the Thai FDA Re: Certificate of manufacturing premises for food importation in cased of imported dietary supplements.

Step 2: Evaluation process. Applicant has to fill the application form and submit together with all scientific documents to the Thai FDA. Several aspects regarding the product shall be considered for evaluation such as quality, safety, efficacy, claims, labelling and advertisement approval (ACCSQ-TMHS, 2006)[123]. Additional documents may be requested during the evaluation process that also will extend the timeline for evaluation, as necessary.

[122] Clause 4(1) of the notification of the MoPH No. 293 B.E. 2548 (2005)
[123] ACCSQ TMHS, 2006, p. 14-15

Step 3: Record keeping. After approval, all application forms including related documents shall be safely kept for post-market monitoring. In case that any approved document is lost, the applicant shall notify at the police station and take a copy of notification to apply for the copied application from the Thai FDA.

In case of any dietary supplement registered and sold on the market before the Notification of No. 293 is legally effective, the FBOs shall also register this product by submitting documents which demonstrate that the product has been registered before the date of enforcement and all contained ingredients still are the same. If any change on an ingredient or a label of the dietary supplement, the FBOs shall apply the new process with all previous approved documents and scientific evidences supporting that the new substance is safe and efficient for consumers while the claims and label are reliable and not misleading.

On the other hand, a new micronutrient which is not included in the positive list or a new dietary supplement[124] shall be applied for label approval before placing the product on the market. The Thai FDA issued the notification of the Thai FDA (T. FDA, 2006a) to establish a list of evidences and documents needed for application of the label approval which can be summarised as follows:

1. Documents indicate details of raw material specifications which are active ingredients such as scientific names and their characterisation, method of quality consistency control and test method of raw material identity, and analytical methods of the active substances or marker with specification of those substances in raw materials, in case of claims for quantity of the active substances.

2. Documents indicate product specification including details of supplement formula by declaring unit or weight in percentage of all ingredients and separating active ingredients and excipients respectively.

3. Documents indicate details of production process steps according to real production.

4. Result of analysis regarding the supplements shall be reported by governmental offices, or officially authorised or certified agency, or organisation from authority in that country, or certified by international laboratory accreditation body or from other institutes that are prescribed by the Food Committee. The result shall examine quality and safety aspects including pathogenic microorganisms, contaminants, quantity of micronutrients which are active substances regarding the product claims.

5. Certificate of manufacturing premises, in case of imported dietary supplements.

6. Certificate of free sale, in case of imported dietary supplements.

7. Scientific evidences to support that ingredients contained in dietary supplements are safe and have history of use as food originally.

8. Label of the product in Thai or English language. In case of other language, the translation version shall be included.

The approval procedure is mostly similar to the process of product registration but the timeline depends on scientific sound of above documents.

[124] Clause 4(2) of the notification of the MoPH No. 293 B.E. 2548 (2005)

2) Maximum safe level of vitamins and minerals

In the positive list, the maximum limits of micronutrients contained in dietary supplements are determined on the "Thai Recommended Daily Intakes for age of 6 years and up (Thai RDI)" basis. The Thai RDI was established by the Thai FDA to be reference values of nutrition labelling for general Thai healthy people based on the Recommended Daily Dietary Allowances for Healthy Thai (Thai RDA). Vitamin or mineral contents shall not be less than 15% and not exceed the Thai RDI[125] which were listed in 1989 for 17 nutrients including micronutrients needed for daily intake of 8 different age groups in Thai population. To set up the Thai RDI, the highest values recommended for persons between 20 to 29 years of both genders are chosen. Moreover, other relevant values are also considered such as Daily Values (DV), Daily Reference Values (DRV), and Reference Daily Intakes (RDI) which are prescribed by U.S. FDA, and Nutrient Reference Values (NRV) which are proposed by Codex Alimentarius (T. FDA, 1998)[126]. It has been obviously emphasised that the Thai RDI is for general healthy Thai people, not patients, infants pregnant women, or other groups whose nutrients demand are different from the normal group as well as the consumption of prescribed food shall be of 5 major essence food groups. Therefore, a warning statement relating to consumption of essential foods is fully mandated to avoid misleading usage of dietary supplements.

3) Other safety requirements for product perspective

Other standards related to dietary supplements are required[127] as follows:

1. Pathogens in dietary supplements shall not be exceeded than the maximum limits[128] as follows;

- *Escherichia coli* shall less than 3 per 1 g of food by Most Probable Number (MPN) method,

- Absence of *Staphylococcus aureus* in 0.1 g of food,

- Absence of *Clostridium* ssp. in 0.1 g of food, and

- Absence of *Salmonella* ssp. in 25 g of food

2. Contaminants (e.g. microbial toxins, pesticide residues, other toxic substances, chemical contaminants, and veterinary drug residues) shall not exceed the permitted limits in the relevant Notifications of the MoPH and Announcements of the Thai FDA.

3. Food additives contained in supplements shall be complied with the notification regarding food additives.

4. Packages or containers used for these products shall follow to the Notification of MoPH, Re: Packaging.

[125] Clause 4(5) of the notification of the MoPH No. 182 B.E. 2541 (1998)
[126] The notification of the MoPH No. 182 B.E. 2541 (1998)
[127] Clause 5 – 6, and 8 of the notification of the MoPH No. 293 B.E. 2548 (2005)
[128] Clause 5(2)-(3) of the notification of the MoPH No. 293 B.E. 2548 (2005)

3.2.3.2 REQUIREMENTS OF PREMISES PERSPECTIVES

Similar to other food products, all establishments of dietary supplements shall be complied with the quality control assurance based on GMP requirements under the Notification of the MoPH No. 193 B.E. 2543 (2000), No. 239 B.E. 2544 (2001), and revised notification No. 318 B.E. 2553 (2010) Re: Production Processes, Production Equipments, and Foods Storages before producing the products[129]. The GMP requirements based on the Codex guidelines[130] consist of 6 areas covering all the production chain as follows (T. FDA, 2000)[131]:

1. Location and manufacturing buildings;

2. Tools, machineries and production equipments;

3. Control of production process;

4. Sanitation;

5. Cleaning and maintenances; and

6. Personnel and hygiene workers.

For any imported dietary supplement, a certification of premises is required to submit to the Thai FDA before the products are allowed to import and launch the national market. In accordance with the announcement of the Thai FDA regarding the certification of premises for imported foods (T. FDA, 2001)[132], the establishments shall be complied with the national GMP requirements or equivalent to one of these following quality assurance systems:

1. General Principles of Food Hygiene established by Codex Alimentarius; or

2. HACCP system; or

3. Quality Management System based on ISO; or

4. Other quality assurance system which is equal to 1-3.

The above certificate shall be approved by either the national competent authority, an officially certification agency, or any institute accredited by international agency. To submit the Thai FDA, an original certification and, in case of other than Thai and/or English language, translated version approved by the embassy of manufacturing country or international organisations shall be provided. If the original version is not available, a copied certificate which is authorised by the national competent authority, an officially certification agency, or embassy of manufacturing country is acceptable.

[129] Clause 7 of the notification of the MoPH No. 293 B.E. 2548 (2005)
[130] General Principles of Food Hygiene of Codex Alimentarius (CAC/RCP 1-1969)
[131] Attachment of the notification of the MoPH No. 193 B.E. 2543 (2000)
[132] Announcement of the Food and Drug Administration, Re: Certification of premises for imported foods

3.2.3.3 REQUIREMENTS OF PRESENTATION PERSPECTIVES

Food which is labelled in order to deceive or try to deceive the purchasers in matters of quality, quantity, usefulness or special nature or place or country of production shall be adulterated that is not able to produce, import or distribute for sale in the territory[133]. Therefore, the label is one of documents needed for application of a food product licence[134]. Moreover, false or deceptive advertising of the quality, usefulness or indication of a food is prohibited[135] and all advertising materials related to food such as radio, television, film, newspapers or other printed matter shall be approved by the Thai FDA before publication[136]. Micronutrient supplements are also required to comply with relevant regulations with their presentation in order to avoid consumer from misleading information and misuse of the products.

1) Labelling

Under relevant regulations[137], labelling of dietary supplements can be classified into 3 types resulting in different requirements needed. Specific requirements of each type can be summarised as follows;

Type 1: Labelling of dietary supplements which is directly sold to consumers. Full information regarding product contents, place of production, and warning statements shall be honestly present on the label as following items:

1. Thai language (and English language, as applicable)

2. Product name with indicating "Dietary supplement"

3. Food serial number

4. Name and address of manufactures, importers, or distributers (In case of importer, the country of origin shall be labelled)

5. Quantities and units of dietary supplement depending on its characterisation (tablet as number per pack, liquid as net volume, or solid as net weight)

6. Name and quantities of active ingredients regarding its claims

7. Declaration of "utilizing preservatives" (if any)

8. Declaration of "natural colour added", or "artificial colour added" (if any)

9. Declaration of "natural fragrance", "imitate natural fragrance", "synthetic fragrance", "natural flavour", or "imitate natural flavour" (if any)

10. Declaration of "name of sweetener" (if any)

---

[133] Section 25, 27 of the Food Act B.E. 2522 (1979)
[134] Section 35(4) of the Food Act B.E. 2522 (1979)
[135] Section 40 of the Food Act B.E. 2522 (1979)
[136] Section 41 of the Food Act B.E. 2522 (1979)
[137] Clause 9-10, and 12 of the notification of the MoPH No. 293 B.E. 2548 (2005) and the Notification of the MoPH No. 309 B.E. 2550 (2007) Re: Dietary supplements (2nd edition)

11. Declaration of "Oxygen Absorber contained" by red letter at least 3 mm. size with white background (if any)

12. Clear statement of "should regularly eat different varieties of full 5 categories of food, in an appropriate proportion" with bold letter which colour of the letter contrast with background of frame of wording state that "No effect for prevention or cure disease"

13. Manufacturing date, expiry date or best before (in a case basis). If a minimum durability of the product is no longer than 90 days, date, month, year of expiration shall be labelled, in contrast, only moth and year of expiration shall be required in case that its shelf-life is more than 90 days.

14. Instruction for use

15. Instruction for storage (if any)

16. Clear warning statements, particularly in dietary supplements containing micronutrients;

- "Do not use by infants, children, and pregnant" by text size shall be not smaller than 1.5 mm addressing in the text box with background colour in contrast to the package colour.

- "Do not use for weight reduction", in case the product consists of sweetener. An additional statement as "Phenylketonuria, this product contains phenylalanine" shall declare if Aspartame is included.

- "Do not take more than the Thai RDI" in case the product claims on health or nutrition.

Type 2: Labelling of dietary supplements which is indirectly sold to consumers. Above information item 1 - 5 are required for this type of label.

Type 3: Labelling of dietary supplements which is produced for export only. There are three elements required on the product label, however other information may be necessary based on the requirement of each importing country;

- Any language is able to use;

- Country of origin; and

- Food serial number.

It has been obviously presented that the label of dietary supplement which is directly sold to consumers requires many information more than other types.

2) Claims

Any dietary supplement which intently presents nutrition claim, utilise food value in sale promotion, or define a specific consumer group in sale promotion shall provide a nutrition labelling (ACCSQ-TMHS, 2006) in Thai language and another language, as applicable. However, this requirement shall not mandate to a

supplement which is neither directly sold to consumers nor produced or imported for sale in the country. FBOs shall follow the criteria for nutrition claims[138] which classifies into 3 categories:

1. Nutrient content claim refers to any claim of nutrient or energy level in that product such as "source of calcium", "rich in vitamin B". However, the claims of "Free" or "Low" shall not be allowed to use, if that product or natural content of that product conforms to condition without being passed through any special process or product development.

2. Comparative claim is the comparison of quantity of nutrient or energy of at least two kinds of products, e.g. "less than or fewer", "reduced", "enriched". Under this claim, "a reference food" used as a baseline to compared the claimed product shall be complied either of following categories; 1) Producer's own normal formula product; or 2) Same kind or similar product, which present such a food in general and to be sold in domestic market. It is important to note that the comparative claim shall prohibit if the quantity of the reference food has nutrient or energy which conform to "Low "or "Less" condition. To present the comparative claim on the product label, type of nutrient, percentage of comparison, and the quantity of nutrient per serving size shall be noticed.

3. Nutrient function claim includes any claim of function of nutrient to human body based on following conditions;

- Nutrients shall be in the list of Thai RDI[139]

- The nutrient content of the claimed product shall be classified as "source of" in the level of reference serving size or per 100 g or 100 ml of product.

- The claim shall not be provided for a specific product claim

- The claim shall be based on reliable scientific evidence

- The claim shall not be expressed or meant to lead consumers to understand that the consumption of such nutrient is able to prevent or cure of any disease.

The nutrient functional claim shall be approved by the Thai FDA before applying in the product label. The permitted claims were listed and announced in 2008 (T. FDA, 2008b)[140]. Examples of allowed nutrient function claim such as "Vitamin B_1 and B_2 assist in function of nervous system", "Calcium is the important composition of bones and teeth", "Folate is an important composition to build red corpuscle".

Conditions of nutrient content claims and the comparative claims can divide to two criteria based on the quantity of the claimed nutrients. In the first criteria, the nutrient claim may be displayed by using the quantity of reference serving size in case such a nutrient and its unit listed in the Appendix No. 2, so the nutrient claim shall conform to the condition in the table 1 of the Appendix 4. On the other hand, the nutrition claim based on per 100 gram or 100 of food shall be displayed if the nutrients are not complied with the first criteria. For vitamins and minerals, nutrient content claims and the comparative claims of two different criteria can be summarised as below table:

[138] Appendix No.4 of the notification of the MoPH No. 182 B.E. 2541 (1998)
[139] Appendix No.3 of the notification of the MoPH No. 182 B.E. 2541 (1998)
[140] Announcement of the Food and Drug Administration, Re: declaration of nutrient function claim

Table 8 Summary of conditions of nutrient content and comparative claims base on two different criteria

Claim	Type of criteria	Specific condition
1. Good source, contains, provides	1. Nutrition Claims per Quantity of Serving Size	The nutrient shall be of 10 to 19% of Thai RDI*
	2 Nutrition Claims per 100 g. or 100 ml of food	**Solid form** - Shall not less than 15% of Thai RDI* per 100 g. of food; or - Shall not less than 5% of Thai RDI* per 100 kilocalories. **Liquid form** - Shall not less than 7.5% of Thai RDI* per 100 ml. of food; or - Shall not less than 5% of Thai RDI* per 100 kilocalories.
2. High, rich in, excellent source of	1. Nutrition Claims per Quantity of Serving Size	The nutrient shall be of 20% and up of Thai RDI
	2 Nutrition Claims per 100 g. or 100 ml of food.	**Solid form** - Shall not less than 30% of Thai RDI* per 100 g. of food; or - Shall not less than 10% of Thai RDI* per 100 kilocalories. **Liquid form** - Shall not less than 15% of Thai RDI* per 100 ml. of food; or - Shall not less than 10% of Thai RDI* per 100 kilocalories.
3. Increased, more, added, fortified, enriched	1. Nutrition Claims per Quantity of Serving Size	When compared to the reference food, if the nutrient content in this food is higher than in reference food, the different of quantity shall not be less than 10% of Thai RDI*
	2. Nutrition Claims per 100 g. or 100 ml. of food	**Solid form** - Increased vitamins or minerals from 10% and up, compared to reference food. The different quantities shall not less than 10% of Thai RDI* of those vitamins or minerals. **Liquid form** - Increased vitamins or minerals from 10% and up compared to reference food. The different quantities shall not less than 10% of Thai RDI* of those vitamins or minerals.

Remark: * refers to the Thai Recommended Daily Intakes for ages of 6 years and up.

In case of claims expressing about health such as "healthy, healthful, healthiness" or similar declaration, quantity of serving size of that product shall consist of Protein, Dietary fibre, vitamin A, B_1, B_2, Calcium, and Iron at least 10% of Thai RDI.

Any health claim on label shall be followed the notification of MoPH regarding health claims and warning of food consuming[141], however the notification is still on the process of draft development based on the Codex guidelines[142] . Therefore, currently, health claims displayed on supplement label shall be approved by the Thai FDA on a case-by-case basis and criteria on Appendix no. 4 of the Notification of the MoPH No. 182 B.E. 2541 (1998) (T. FDA, 1998)[143].

3) Advertisement

Any false or deceptive advertising of the quality, usefulness or indication of a food is prohibited[144] and all advertising materials related to food such as radio, television, film, newspapers or other printed matter shall be proven by the Thai FDA before publication[145]. If FBOs violate the requirements under Section 40, they shall be liable to imprisonment of not more than 3 years or fine of not more than 30,000 baht or both[146], while they shall be fined or not more than 5,000 baht in case of infringement of section 41[147]. The statistic data of Thailand[148] presented that an average monthly income per household was 23,236 baht in 2011. Therefore, the Thai FDA officially notified the criteria on adverting foods in 2008 (T. FDA, 2008a)[149]. Advertisement defines to any activity to convey information to public for direct or indirect promotion of the product or service. In principle, the advertisement shall be truthful and not misleading to consumers. Contents of the advertisement shall not overstate scientific evidences. In case of nutrition and health claims, only permitted claims can apply to the products, on the other hand, in case of any claim other than the list, relevant scientific information shall be submitted for advertising evaluation and approval before addressing on food products.

General criteria on advertising foods covers name of product, statements, and picture or image used in the advertisement through all public media such as printing matters, radio broadcasts, televisions, screens, movies, or internets. Any visual performance or statement shall not influence misunderstanding to public based on the relevant requirements. Moreover, a compulsory statement for advertising dietary supplements is "This product is not intended to prevent, treat or cure human disease" shall be addressed in the advertisement. Apart from the requirements based on the Food Act B.E. 2522 (1979), there are other relevant regulations regarding food advertisements such as the Consumer protection Act, B.E. 2522 (1979), the Radio Communication Act B.E. 2498 (1955), and the Administrative Act B.E. 2539 (1996).

An example of presentation of dietary supplements sold in the Thailand market which is complied with all mandatory requirements is as a below figure:

[141] Clause 11 of the notification of the MoPH No. 293 B.E. 2548 (2005)
[142] CAC/GL 23-1997
[143] Guidance on Thai FDA implementation on claims related to foods
[144] Section 40 of the Food Act B.E. 2522 (1979)
[145] Section 41 of the Food Act B.E. 2522 (1979)
[146] Section 70 of the Food Act B.E. 2522 (1979)
[147] Section 71 of the Food Act B.E. 2522 (1979)
[148] The National Statistical Office, Ministry of Information and Communication Technology, http://web.nso.go.th/index.htm
[149] Announcement of the Food and Drug Administration, Re: Criteria on advertising foods B.E. 2551(2008)

Figure 12 Presentation of dietary supplements which is directly sold to consumers (1-9, 11-16 items of Type 1 labelling)

3.2.3.4 PROBLEMS AND CHALLENGES IN REGULATIONS AND PRE-MARKET CONTROL SYSTEM

Confusion between drugs and dietary supplements has been troubled for all stakeholders. Although they are regulated and controlled separately by either Drug Act or Food Act, it sometimes hardly distinguishes due to similarity of ingredients, dosage forms, and packages. A critical point to decide whether medicine or dietary supplement is the intention of the FBOs to sale that product, if purpose of usage is for diagnosis, treatment, relief, cure or prevention of human or animal diseases or illness, the product containing micronutrients shall be classified to drug and strictly complied with the Drug Act (Isichaikul, 2002)[150].

Even the maximum limit and positive list of micronutrient are set for dietary supplements, the level of each micronutrient is not considered on other food sources resulting in unintentional over-consumption that may cause health problems. One of examples is Iodine which is lawfully required to fortify to fish sauce, soy sauce, so consumers may take over amounts of Iodine accumulated from both supplements and other food sources. Moreover, the positive list is not frequently up-to-date, comparing to the innovative technology and new dietary supplements which constantly launch into the market. Main reasons of this problem are that scientific information is inadequate to support and consider a new substance contained in the supplements while a unique and independent risk assessment body like EFSA is essentially required. Therefore, in some issues, the requirements are not comprehensive for all supplements that should be considered and evaluated on a case-by-case basis.

From the viewpoint of the presentation perspective, problems on nutrition labelling of dietary supplements can be evaluated to 3 aspects (Teerawat, 2002)[151]. Firstly, problems related to the product are mostly from claims and their presentation on the product label, excluding quality and safety of the products. For examples, a reference amount of supplement is not yet determined under the Notification No. 182, nutrient contents based on 100 g or 100 ml of the product, therefore, are applied for calculation

[150] Chapter 3
[151] Chapter 3

resulting in over amounts of nutrients showed on the labelling. Permitted claims on nutrient content and nutrient function are limited for dietary supplements which are continuously researched and developed. Secondly, consumers have inadequate knowledge or information related to nutrition, for example, nutrient amounts and its calculation, and reference value of the Thai RDI. The last aspect is from FBOs, especially who intend to advertise misleading information and claims to make their business profits while the competent authorities cannot completely prohibit all unproven products. Besides, the advertising dietary supplement is one crucial problem in Thailand, even though all advertisements shall be pre-approved by the Thai FDA with supported documents. It has been shown that many advertisements of supplements currently found in the market are not permitted yet, especially in direct sale market, while claims presenting on these advertisements mostly mislead to consumers (Khaopolsri, 2004)[152].

3.3 Summary

In brief summary, according to regulations and requirements of pre-market control implemented in EU, US and Thailand, It has been obviously shown that there are different measures applying to control food supplements, particularly in US. The DSHEA of 1994 gives more freedom for FBOs to produce, import, distribute, or sale supplements on the market leading to enhance product development, innovative technology of production, and new ingredients. The FBOs shall ensure that the products are safe and complied with relevant regulations but the burden of proof on compliance is mainly responsible by the U.S. FDA. In contrast, EU and Thailand have stricter rules for supplements before selling them to the market. The positive list of permitted micronutrients is a tool of safety and efficacy assurance, while any new substance shall be evaluated on the risk assessment basis and approved by the competent authorities. Abundant evidences on scientific base are necessary to submit for the approval of the new substance before applying in food supplements and placing on the market. Therefore, it is time-consuming process for both FBOs and the authorities.

In EU, US, and Thailand, quality management systems such as GMP and HACCP principally apply to all premises of food supplements. The establishments shall be registered by the competent authorities before producing products. For the presentation perspective, all EU, US and Thailand highly concern on requirements for labelling, product claims, and advertisements in order to prevent consumers from misleading information and giving an appropriate choice for the consumers. The presentation also shall provide noticeable statements to distinguish between the food supplements and medicinal products.

Even different requirements regarding food supplements are regulated, codex standards are regularly adapted for developing these specific regulations at national levels in EU, US, and Thailand, as well as the concept of risk analysis is a fundamental basis for establishments of requirements and relevant measures for food supplements in these three countries. More comprehensive comparison would be enlightened in the chapter 5 of this thesis.

[152] Chapter 3

4. POST-MARKET CONTROL SYSTEMS

The FAO/WHO guidelines (FAO/WHO, 2003) define food control as "a mandatory regulatory activity of enforcement by national or local authorities to provide consumer protection and ensure that all foods during production, handling, storage, processing, and distribution are safe, wholesome and fit for human consumption; conform to safety and quality requirements; and are honestly and accurately labelled as prescribed by law". Therefore, the food control system consists of food law& regulations and enforcement activities before and after food products are sold to consumers. To monitor the food products comply with food regulations and relevant requirements, a food inspector plays an essential role in the food control system by inspecting premises and processes for compliance, sampling food during harvest, processing, storage, transport or sale to establish compliance and contribute data for risk assessments as well as identify offenders. In addition, collecting evidence, carrying out inspection, sampling and certification of foods both domestic production and importation are taken by the food inspector according to the food laws. Thus, activities of post-market control are important to achieve goals of the food control and consumer protection.

Since food supplements are classified as foods, activities of post-market control are also applied by official food inspection services to ensure that the products are still safe and compliance with relevant requirements while non-compliant products are found and removed from the market and consumers. Activities of post-market control are such as developing monitoring and surveillance programmes. The Codex guidelines (Codex, 2008)[153] state that a monitoring is the act of conducting a planned sequence of observation parameters to assess whether a control measure is under control. It includes collection and analysis of data derived from surveillance of clinical disease in humans, epidemiological investigation of outbreak and other studies, surveillance based on laboratory tests of hazards in the products, data on environmental hygiene practices and procedures. Under the FAO/WHO definition (FAO/WHO, 2003)[154], surveillance is the continuous monitoring of the food supply to ensure consumers are not exposed to components in foods, such as chemical contaminants or biological hazards which pose a risk to health. Therefore, both monitoring and surveillance programmes support the food inspector to plan work efficiently and decide appropriated control measures based on scientific evidences resulting in effectiveness of the post-market control system. Apart from monitoring and surveillance plans, other activities of the post-market control are sampling and testing products, implementing product withdrawal or recall measures, punishing FBOs and relevant stakeholders, establishing information exchange system, enhancing capacity of competent officers & FBOs, and promoting consumer educations.

This chapter focuses on enforcing regulations and relevant measures on post-market control of the food supplements. Procedure and results of monitoring and surveillance programmes are described and showed how the effectiveness and challenges of these requirements controlling unsafe products are. Since most of information is official documents for authority officers, available sources and accessibility is limited, especially in Ireland and US. Therefore, the development of annual monitoring and surveillance plan for foods and dietary supplements in Thailand is described in detail giving an example for a more understanding.

[153] CODEX, 2008, CAC/GL-69-2008.
[154] Annex 1 of the FAO/WHO Guidelines

4.1 EU (Ireland case study)

Under the GFL, the FBOs take charge of producing safe food and shall follow obligations after placing any food product on the EU market, such as responsibilities of withdrawal and recall unsafe products from the internal market. Establishment of traceability system based on "one-step backward one-step forward approach" shall be placed along supply chain of the supplements. Apart from the GFL, the regulation (EC) No. 882/2004 lays down general rules for consistent performance of official controls in 27 MSs to enforce food law, monitor and verify that the relevant requirements are fulfilled by FBOs at all stages of food chain. This provision applies for both food and feed, except agricultural products[155], in order to prevent, eliminate or reduce any risk to acceptable levels for humans and animals, either directly or through the environment, to support fair practices in feed and food tread, and to protect consumer health including given information[156]. Each MS shall perform official controls by designing competent authorities, specifying tasks related to official controls, providing correct procedures to staff, and informing all control activities based on transparency and confidentiality. The designed official controls implement not only in all MSs, but also the third countries who export food products to the EU market. Activities are such as inspections of raw materials, semi-finished products, food contact materials, labelling, presentation, and advertising, Audits of hygiene condition in FBOs[157], establishment of sampling and analytical methods[158], including enforcement for non-compliance in both normal and crisis situations. In Ireland, the Food Safety Authority of Ireland (FSAI) plays a major role under the FSAI Act of 1998 to provide both national requirements and official controls for food safety as appropriate to comply with relevant regional provisions. Therefore, enforcement in Ireland are carried out by the FSAI[159] collaborating with other official agencies under the service contracts and granted power[160](FSAI, 2012d). In addition, the Statutory Instruments on European communities (Official Control of Foodstuffs) S.I. No 117/2010 and S.I No. 344 of 2011 have come into force to support the Regulation EC No. 882/2004. The regulation S.I. No 117/2010 addresses official measures to control and manage non-compliance in relation to the EC regulations. Procedures on communication and enforcement are clearly indicated under this provision. A guilty person is legally liable on either summary of conviction or conviction on indictment[161], while the S.I. No 344 of 2011 amended the previous provision by regulating that FBOs responsible for the non-compliance with food legislation shall pay the charges from additional controls exceeding the normal control activities[162].

Under Article 15 of the Directive 2002/46/EC, all MSs shall bring into force the law, regulations, and administrative provisions necessary to comply with this directive. It means some requirements of post-market control for food supplements are depended on the national legislation. In Ireland, therefore, the enforcement provision of food supplements is issued under part 3 of the European Communities (Food Supplements) Regulations 2007 (S.I. No. 506 of 2007) and amended in the European Communities (Food Supplement) (Amendment) Regulations 2010 (S.I. No. 355 of 2010). These provisions including other legal

[155] Article 1(2) of the regulation (EC) No. 882/2004
[156] Article 1(1) of the regulation (EC) No. 882/2004
[157] Article 10 of the regulation (EC) No. 882/2004
[158] Article 11 of the regulation (EC) No. 882/2004
[159] Section 49 of the FSAI Act of 1998
[160] Section 50-51 of the Act of the FSAI Act of 1998
[161] Part 5 of the S.I. No. 117/2010
[162] Section 3 of the S.I. No. 344 of 2011

requirements are applied in Ireland by relevant competent authorities for the purposes of ensuring compliance with these regulations[163].

4.1.1 Inspection and sampling procedure

Under the enforcement provision in the Irish Regulations of food supplements, a sampling procedure is established for both domestic and imported food supplements sold in the Irish market. All samples shall be analysed and certified by the official laboratories if they comply with requirements. However, any protective measure such as withdrawal or recall will immediately apply in case of non-compliance and the FBOs shall be punished. The sampling and enforcement procedure are summarised as below table:

Table 9 Summary of enforcement procedure of food supplements sold in the Irish market

Step	Action	Responsible person
1. Sampling	- open any container and take or purchase a sample of food supplements or of another relevant article or substance without payment	An authorised officer
2. Sample preparation	- In case of practicable division, divide the sample into three approximately equal parts. - In case the product container is unopened and its division is not reasonably practicable, or may affect the composition or impede the proper analysis of the samples, take three lots of products as samples - Mark and seal all samples in such a manner as its nature.	An authorised officer
3. Sample distribution	- Send each part of samples to an official laboratory, and seller. Retain one part to the office	An authorised officer
4. Sample analysis	- Analyse the received sample as soon as possible following the requirements	An approved examiner
5. Result of analysis 5.1 Compliance	- Certify the result of analysis to the person who submitted the sample. The form of Certificate of analysis is as schedule 3 of the Regulations 2007.	An approved examiner
5.2 Non-compliance	- Write the report of non-compliance and send its copy to the FBOs	An authorised officer
	- Remove, detain, or directly withdraw the product from the market and notice to FBOs within 15 days from the date of the detention of the sample	
	- Apply to a judge of the District Court for an order directing that such products be destroyed or disposed of	
	- Order to destroy or dispose the products if they fail to	A District court

[163] Article 8(3) of the S.I. No. 506 of 2007

Step	Action	Responsible person
	comply with these regulations not exceeds 14 days.	officer
	- Destroy or dispose the products according to the order of the District court, and notify to FBOs	An authorised officer
	- Require a person to state name and address, in case it has reasonable evidence that such person has violated any provision of these rules	An authorised officer
6. A guilty of defence	- A person who is guilty of an offence shall be liable for punishment. The person includes anyone who; • Fails to comply with any request or notice from the authorised officers based on these regulations; • Gives any information or corroborative evidence which is false or misleading; • Forges or utters a certificate of analysis or other documents purporting to be issued; • Alters with intent to defraud or deceive a certificate of analysis or other documents purporting to be issued; • Has in possession a forged or an altered document without lawful authority; • Intent to defraud or deceive tempers or interferes with any samples taken under these regulations • Falsely represents himself or herself to be an authorised officers - An authorised officer or an approved examiner acting in his or her duties to these regulations is not a guilty of defence	
7. Punishment	- Prosecute an offence to a guilty person - Every contravention shall be separated and shall carry the same penalty as for a single contravention - Fine a person who is guilty of an offence in case; • On summary conviction to a fine not exceeding €5,000 or at the discretion of the Court to imprisonment for a term not exceeding 6 months or both, or • On conviction on indictment, to a fine not exceeding €500,000 or imprisonment for a term not exceeding 3 years or both. - Additional Fine a person who is guilty of an offence in case there are special or substantial reasons decided by the court for cost and expenses in relation to taking of samples, carry out of tests, examination and analyses and in respect of the remuneration and other expenses of employees, consultants and advisors incurred by the FSAI or official agency.	An authorised officer from The FSAI or, an official agency or both

4.1.2 Monitoring and Surveillance programmes

The FSAI is mainly responsible for the enforcement according to food legislations in Ireland through service contracts with following 33 official agencies (FSAI, 2011); 28 local authorities; the Health Service Executive; the Department of Agriculture, Food and the Marine; the Sea-Fisheries Protection Authority; the National Standards Authority of Ireland; and the Marine Institute. By the service contract, the Integrated Multiannual National Control Plan (MANCP) for 2007-2011 (FSAI&DAFF, 2007)[164] has been placed at national level which comprehensively covers control of food, feed, animal welfare, and animal and plant health including the food supplements. Moreover, the MANCP for 2012 – 2016 has also developed and submitted to the EC.

4.1.2.1 PRODUCTS AND PRESENTATION PERSPECTIVES

Under each MANCP, the compositions of food supplements and their labelling are included in the national surveys of monitoring and surveillance programmes that are carried by the FSAI and the official food control agencies (FSAI, 2009b). According to the national control plan consisting of the sampling and testing procedures, food samples are randomly taken at the time of inspection from food business or retail or wholesale level, and sent them to the food control laboratories for analysis. The testing results will be communicated to the enforcement officers for further implementing appropriate measures as well as to the FSAI for evaluating and formulating a national picture of food control in Ireland and the EU by communicating to the EC. The number of samples may annually vary depended on relative factors such as the testing result of previous years; current and proposed food legislation; new risks and updated toxicological information in relation to the supplements; enforcement action and consumer complaints on suspected supplements from the previous years.

The FSAI annual report 2011stated that 1,879 notifications of domestic and imported food supplements reported to the FSAI were mostly checked for compliance. The number significantly increased from 2010 (FSAI, 2010a)[165] in which a total of 645 food supplements were reported through the new online notification. Under the notification procedure, a label of food supplement including relevant information with the product shall be submitted to the FSAI and they are assessed for compliance against the relevant legislations. It could be assumed that all food supplements and their labels are scientifically assessed not only before placing on the market but they are also controlled after selling in the Irish market through the national monitoring and surveillance programmes. In addition, the herbal supplements survey for irradiated ingredients has been ordinarily checked since 2002 and the results have been annually published through the FSAI website (FSAI, 2012e). Besides, a range of factors such as antioxidants, flavourings, nutrient value in the supplements is also tested for legal compliance, while the monitoring survey on Irish food supplements manufacturers is going to be conducted in 2013[166].

Monitoring and surveillance of food labelling in Ireland are also continuously conducted to assess compliance with the legislations (FSAI, 2012f). For example, a study on consumer's attitudes to food labelling was conducted in 2009 (FSAI, 2009c). The survey investigated understanding, knowledge, and attitude to mandatory food labelling including nutritional labelling and claims from 1,021 consumers, aged

[164] FSAI and the DAFF, 2007, the NCP for Ireland for the period from 1st January 2007 to 31st December 2011
[165] FSAI, 2010, p. 13
[166] Information from the FSAI through electronic mail replied on 17 December, 2012

16 years and older, across Ireland. The result of this survey showed that consumers considering on food labels increased from 8% in 2004 to 25% in 2009, while at least two thirds of respondents would be persuaded to buy food products labelled with a nutrition claim. In 2010, the accuracy of nutrition labelling of pre-packed food in Ireland was surveyed by sampling 98 products to check legal compliance and reliable information regarding the nutritional labelling. However, the food supplement was not included in the product samples.

Apart from competent authorities, the ASAI, an independent self-regulatory body for the advertising standards, provides monitoring and an on-line service for a complaint of market communication both direct and indirect ways as well as all commercial advertising in Irish media such as prints, radio, television, digital media, cinema and outdoor interests relating to public media. A standard code of advertising food supplements has been developed under the section of health and beauty products, and all advertisements regarding the supplements are commonly monitored by this agency. The ASAI Annual report 2011 (ASAI, 2012) showed that the full monitoring programme of commercial communication in the media has been implemented since 2007 and thousands of advertisements are monitored in each year, e.g. 4,000 advertisements in 2009 whereas over 3,500 materials in both 2010 and 2011. It has been demonstrated that all monitored advertisements highly comply with the standard code in excess of 99 percents compliance. Even number of the advertising food supplements were not specifically defined in the report, It may be assumed that most of them comply with the standard code relating to vitamins, minerals, and food supplements[167] which are also consistent with the mandatory requirements. In case of complaints, after receiving a complaint from consumers or public interests through electronic mail, post or online system, it is either solved informally by the secretariat or submitted to the independent Complaints Committee for formal adjudication. The decision of each complaint depends on how the deviation of the advertisement from related standard code is. The ASAI Annual report 2011 indicated that 1,402 written complaints concerning 867 advertisements were received by the ASAI in 2011 which was lower than the submitted complaints in 2010. From the complaints in 2011, there were 104 complaints relating to health and beauty sector which is the fifth group of product complaints. In addition, main areas of complain are generally related to misleading or displeasing advertisements, concerning children, health and safety resulting in fear and distress including health claims and environmental claims. Under considering communication channels, the digital media gave rise to the largest block of complaints because it has been extended for commercial communication since 2009 while the number of complaints regarding other materials such as prints, brochures or leaflets, and direct selling also increased, comparing to the problems in 2010. In the end of 2011, The ASAI dealt with 1,535 complaints consisting of 265 complaints from 2010 and complaints received in 2011 and pending 132 issues of 96 advertisements to be carried forward to 2012.

4.1.2.2 PREMISES PERSPECTIVE

According to the Regulation (EC) No 852/2004 and 853/2004, all establishments handing food products and products of animal origin shall be registered by the competent authority of each MS. A list of approved establishments shall be legally updated and available to other MSs and consumers. In Ireland, the approved food establishments are regularly listed and published on the FSAI website[168]. In addition, the Environmental Health Officers (EHOs) under the Health Service Executive (HSE) by collaborating with the

[167] Section 8.14-8.16 of the ASAI standard code
[168] http://www.fsai.ie/food_businesses/approved_food_establishments.html

FSAI takes responsibility on inspecting manufacture and retail establishments producing or selling food supplements in Irish market while the auditing of compliance of available supplements will come under their remit (FSAI, 2010c). In order to support the inspection work, the checklist for food supplement establishment inspection was developed in 2012 and available on the FSAI website for both official control officers and FBOs (FSAI, 2012c). The HSE Annual report 2011 (HSE, 2012)[169] presented that 27,055 establishments were inspected and 4,437 premises or 16% of all establishments had committed infringements. However, the number of food supplement establishments was not clarified in this report.

4.1.3 Communication and information exchange

In Ireland, the "Safety Net", an intra-network system, has been developed as a communication tool between the FSAI and other official controls. For food supplements, the list of notified products is exchanged from the FSAI to other competent authorities through the Safety Net system. The FSAI Annual report 2011 (FSAI, 2011) presented that a total of 15,471 visitors accessing to this system which was approximately 1,289 per month in average. Moreover, other communication channels are available for the public such as the FSAI website which received 396,797 visitors in 2011 to access publication, legislation, food business information, and complaint service. The FSAI's Facebook, Twitter, and YouTube have continuously increased in popularity during this year because they are proactive channels to interact with wider stakeholders. This annual report also demonstrated that a total of 2,415 complaints were handled by the FSAI's Advice Line which 13% increasing from the previous year. Main complains relate to unfit food, suspected food poisoning, low hygiene standards, and unreliable labelling and advertising. However, the specific food products regarding these complaints were not described.

The information exchange in relation to food incidents and alerts was handled by the FSAI and relevant authorities based on a national food incident management plan established in 2002. In 2011, there were 396 food incidents in Ireland which was 12% increase from 2010, whereas 29 food alerts relating to 25 incidents were nationally issued. Most of incidents and national food alerts relate to microbiological hazards but a problem in relation to food supplements was not reported.

Under the RASFF network which mandates all MSs to communicate with the EC[170], the Consumer Protection Division of the FSAI is responsible for the national control point of RASFF (DG SANCO, 2010). The FSAI issues an alert notification based on industry recalls or withdrawals, enforcement activities, surveillance sampling, and consumer complaints while the RASFF information is communicated with relevant official agencies, food industries, and consumers through electronic mail, fax, SMS/text message, press release, where appropriate, and the FSAI website. Moreover, the FSAI by collaborating with other stakeholders develops an action plan or any preventive measure regarding the notification to prevent consumers from the risk as well as provides training and simulation exercises. In addition, the information from alerts and incidents is used as a scientific resource for re-evaluating surveillance and enforcement plans at national and local levels for proactive avoidance. The FSAI annual report 2011 (FSAI, 2011) showed that 46 notifications in respect of food and food contact materials were issued under the RASFF but a specific type of food was not elucidated.

[169] HSE, 2011, p. 31.
[170] Article 50 of the Regulation (EC) No. 178/2002

From a total of 3,812 notifications transmitted through the RASFF in 2011 at the EU level (EC, 2012d), 138 notifications related to the category of dietetic foods, food supplements, and fortified foods (DG SANCO, 2012)[171]. The RASFF Annual report 2011(EC, 2012d) presented that heavy metal contaminants found in food supplements were issued in the RASFF because they are not authorised in the supplement. For examples, lead was reported in the supplements containing clay or in silica capsules migration of chromium. Nickel and manganese were detected in food supplements imported from US. Another major notification from the RASFF relating to food supplements in 2011 included hazards from compositions of the product which are quite often not labelled. Examples of these notifications are unauthorised supplements containing herbal extracts, and unauthorised substance which is contained in the supplements in all forms and colours that are offered to the consumer claiming to have a certain health or other benefit like slimming, aphrodisiac, etc. Moreover, problems on too high content of micronutrients in the supplements were also notified in 2011 such as high content of zinc (453 - 227.9 mg/item) in the supplement imported from US, and high content of selenium (164 µg/item) in the supplement from UK. These products were immediately withdrawn from the market after the alert notifications were circulated to all MSs via the RASFF network. In case non-compliant products are found at the port of entry, they are rejected for placing in the internal market. They may be either delivered back to the country of origin or destroyed at the port of entry depending on the level of consumer risk and case-by-case basis.

4.1.4 Empowerment of competent officers, FBOs and consumers education

The FSAI has regularly updated publications regarding food safety such as codes of practices, guidance notes, training guides in order to facilitate competent officers and FBOs to comply with relevant regulations as well as to educate consumers. For food supplements, many publications are available on the FSAI website such as Guidance Note No.21: Food Supplements Regulations and Notification (Revision 1) in relation to two additional documents, namely; Aide Memoire for Food Supplement Establishment Inspections and; Checklist for Food Supplement Establishment Inspections, providing all information of legislations, legal requirements, and enforcement; The Information on Nutrition and Health Claims and Food Supplements published in 2010 to support correct requirements on food labelling, nutritional labelling and claims for food supplement. A list of Questions and Answers relating to food supplements is provided on the website to enhance consumers' trust and self-protection. Moreover, annual reports, audit reports, survey reports, and other scientific reports are also accessible from the FSAI website.

Apart from publications, the FSAI commonly arranges training programmes and seminars for official agency staff on food control to reinforce enforcement activities and to assist the FBOs for a more understanding on technical requirements and compliance of relevant regulations.

4.1.5 Limitation and challenges on post-market control system

Major problems of food supplements found in the Irish market include unapproved labels with nutrition and health claims; a large variation between the actual value of a nutrient present in the product and the declared value on the label; and unpermitted medicinal substances contained in the supplements which are approximately 10-30% of all notified supplements[5]. However, more information regarding the limitation of post-market control is difficult to access because most of enforcing information is disseminated through intra-

[171] DG SANCO, RASFF Portal version 2012.

network system, while the requirement of pre-notification of product and its label would be a proactive mechanism of pre-assessment resulting in reduction of the post-market work. This pooled information is also a useful source of database for competent authorities to work in monitoring and surveillance programmes leading to have effective plans and appropriate actions.

At EU level, numbers of notifications related to unauthorised ingredients in food supplements are concerned. It has been demonstrated that the major cause relates to the direct accessibility to the consumers through the internet and direct sale market resulting in difficulty for prevention, especially in case the products are sold in the EU often by companies registered outside the EU. Therefore, enhancing consumer awareness for avoiding unverified products is necessary.

4.2 US

In line with the DSHEA law, a manufacturer is mainly responsible for ensuring that dietary supplements are safely produced before reaching consumers without any legal provision on pre-marketing approval. After the supplement is marketed, the U.S. FDA takes action on burden of proof before implementing any measure for consumer protection. The post-market control and other related activities such as monitoring product safety, premises, product information, and scientific research are, mainly taken by the Centre for Food Safety and Applied Nutrition (CFSAN). In addition, results from inspections of supplement manufacturers and distributors, the internet, consumer and trade complaints, occasional laboratory analyses of selected products, and adverse events associated with the use of supplements are also collected for revising monitoring and surveillance programme including preventive measures. Since there is no deviating requirement for dietary supplements from different states, the U.S. FDA implements unique activities on post-market control in all US states and collaborates the Federal Trade Commission (FTC) for controlling advertising supplements, as well as the Department of Justice for criminal sanction.

4.2.1 Inspection and sampling procedure

Since dietary supplements are classified as food products, provisions on enforcement are based on the FD&C Act and amended provisions on Food Safety Law (GPO, 2011)[172] following the FDA Food Safety Modernisation Act of 2011. For dietary supplements, both domestic and imported products are inspected for legal compliance. In addition, the FDA's Compliance Programme for dietary supplements – import and domestic implementation (U. S. FDA, 2011a)[173] has been issued since 2006 and required for implementation as of August 7, 2010 in order to facilitate the FDA officers for conducting activities to evaluate industry compliance with the FD& C Act and other provisions. From this programme, inspections of product, premises, and presentation are involved but the priorities for selecting firms and collecting products should be considered for an effective resource usage.

To inspect domestic and foreign supplement firms, the CGMPs rule is legally applied and priorities of selection are following these orders; 1) firms producing both dietary supplements containing vitamins, mineral, or proteins, and the supplements consisting of other ingredients such as botanicals, animal, and plant extracts, fat and lipid substance; 2) firms producing only supplements containing botanicals, animal, and plant extracts, fat and lipid substance; and 3) firms producing supplement products of vitamin,

[172] GPO, 2011. Public law 111-353-Jan 4, 2011
[173] U.S. FDA, 2011. Implementation Date: 03/26/2010) includes Pen & Ink Changes as of 07/08/10 to Parts I and II

minerals, or proteins. The premises inspection focuses on traditional supplements because of insufficient data on the product safety and bioavailability.

For inspecting samples of product and labels, a sampling procedure differently depends on nutrition labelling and claims on products, as well as specific ingredients in the supplements. Therefore, there are four different areas for the sampling procedures:

Area 1: for general dietary supplements. The sample collection is based on principle of the field exam such as requirement of mandatory labelling, customers, and ingredients. The samples will consist of four original labels and one product container before sending for analysis.

Area 2: for supplements with authorised health claims or nutrition content claims. To comply with certain nutritional requirements, collected sample will consist of 24 consumer size retail packages, 2 packages from each of 12 randomly selected shipping cases or 10% of the number of package in the same inspection lot (collected in duplicate). However, for the imported samples, only 12 retail packages are collected. Collect one package from 12 randomly selected shipping cases or 10% of the number of packages in the same inspection lot (collected in duplicate), whichever is smaller, but do not blend lots.

Area 3: for supplements that may contain cattle materials which are permitted in US. To ensure that the products are not made with prohibited materials, records must be maintained for 2 years and allowed for the U.S. FDA to inspect and copy these documents. In addition, all supporting documents must be promptly submitted to the General Program Contact following completion of the inspection. The permission of product will be made on a case-by-case basis.

Area 4: for supplements containing ephedrine alkaloids. Samples will be collected in maximum of 3-5 samples each consisting of a different lot number including information on the size of each lot sampled on the collection report.

After sample collection by the competent officers, they will be sent to official laboratories to analyse nutrients, and specific ingredients such as Ephedrine Alkaloid. The results will be regularly checked for compliance. In case of non-compliance with greatest concern for public health, either administrative or judicial enforcement action will be considered by the U.S. FDA, whereas an advisory action will be implemented against product of lower public health risk. If the FBOs do not correct violation according to the advisory action, the officer may follow an enforcement action against these FBOs (GAO, 2009). The advisory actions begin from hold regulation meeting with the firm, issue firm a warning, issue consumer alerts, and issue advisory to the industry, respectively. For administrative and legal enforcement actions, working with a company on a voluntary product recall is initiatively provided before applying more strict measures such as detain/refuse the products, pursue legal action against the FBOs, and ban ingredients.

4.2.2 Monitoring and Surveillance programmes

The U.S. FDA is responsible for both monitoring and surveillance programmes. Not only potentially illegal products such as unsafe, false or misleading claims are monitored for compliance, but also information from inspections of dietary supplement manufacturers and distributors, the Internet, consumer and trade complaints, occasional laboratory analyses of selected products, and adverse events associated with the use of supplements that are reported to the agency is collected for developing appropriate programmes.

4.2.2.1 PRODUCT AND PRESENTATION PERSPECTIVES

Reports on adverse event and national survey are important resources of scientific data for monitoring and surveillance programmes of dietary supplements in US because the information regarding product safety from pre-market approval is inadequate. The National Health & Nutrition Examination Survey (NHANES), a nationally representative cross-sectional survey, has been used to monitor the use of dietary supplements since the 1970s and the most recent data was collected during 2003-2006 (Bailey et al., 2011). According to this monitoring programme, it has been shown that 49% of US adult users (n=9,132) used supplements which increased approximately 10% from the survey result during 1988-1994. In both adults and children taking the supplements, multi-vitamin and multi-minerals supplement (a product containing 3 or more vitamins and 1 or more mineral contents) were mostly reported (33% of users), followed by use of botanical supplements (14%). In addition, it has been also revealed that usage of multi-vitamin and multi-mineral supplement has significantly increased, particularly in supplements containing vitamin B_6, B_{12}, C, A, and E as well as supplements consisting of minerals zinc and magnesium. Factors influencing use of dietary supplements were associated with weight status, education, and society, for examples, higher educated consumers were more likely to use supplements while overweight and obese individuals were less likely to take the product. Similar to the NHANES results, the Health and Diet Survey, a national survey sponsored by the U.S. FDA, studied the prevalence of use and reports of adverse events in regard to use of dietary supplements in 2002 (Timbo, Ross, McCarthy, & Lin, 2006). US non-institutionalised aged from 18 years old to adults in households in the 50 states and District of Columbia were interviewed by telephone and 73% of respondents (n = 2,743) consumed dietary supplements in the previous 12 months. Among the user group, 85% were reported taking multi-vitamins/multi-minerals supplement, 77% using a specialised or single ingredient vitamin or mineral supplement, whereas 42% taking other ingredients such as herb and botanical supplements. Moreover, 4% of supplement users had experienced an adverse event resulting from consuming the supplements. The most adverse event reports were associated with multi-vitamins/ multi-minerals (13% of all adverse event reports). From these studies, it may be assumed that the trend of multi-vitamins/ multi-minerals supplement has considerably increased in the U.S market while the supplements integrating single botanical ingredient into multi-nutrients products has also enlarged.

Another tool for collecting adverse event reports is the CFSAN Adverse Event Reporting System (CAERS) developed by the U.S FDA since 2004. Results of monitoring and surveillance revealed that data evaluation and risk assessment is regularly conducted by the U.S. FDA for further inspection and enforcement. According to U.S. statement in 2006 (U. S. FDA, 2006b)[174], during October 2002 - February 2006, 588 domestic inspections of dietary supplement manufacturers were conducted, more than 350 warning letters were issued, products worth more than $13.4 million were seized, and more than $3 million worth of product were voluntarily destructed because of misleading claims, unapproved drug, and unsafe issues. In addition, The U.S. FDA refused more than 4,000 foreign shipments of potentially unsafe or misbranded supplements during the same period. Four years after the statement in 2006, the U.S. FDA addressed in the statement of 2010 (U. S. FDA, 2010)[175] that three areas of dietary supplements posing the greatest risk to public health have been focused on monitoring and enforcement actions as follows:

[174] U.S. FDA, 2006, Testimony: a regulation of dietary supplements, statement as of 2006
[175] U.S. FDA, 2010. Testimony: oversight of dietary supplements, statement as of May 26, 2010.

1) Adulteration with drug substances such as Sibutramine, Viagra, Lovastatin, Synthetic steroids, or steroid-like substances. These products are often sold with misleading labelling and are frequently manufactured without quality controls. Many enforcement actions are taken to protect public health from these illegal supplements such as voluntary recall, press announcements to warn consumers, and criminal persecutions to disrupt the distribution of these products.

2) Unsafe ingredients contained in the supplements such as poisonous or deleterious substance which may lead to harm consumer health. After evaluating adverse events reports and reviewing the medical literatures, a significantly hazardous substance may be found in the adulterated product resulting in withdrawing or recalling these supplements from the market.

3) Illegal claims and unproven claims may persuade consumers to self-treat for a serious disease without the benefit of a medical diagnosis.

To monitor advertising materials, The FTC under Memorandum of Understanding with the U.S. FDA, is responsible to enforce consumer protection laws and regulate dietary supplement advertisements. Both public and non-public investigation are applied for the law enforcement (FTC, 2007). In case a violation of the law occurs, the FTC may consult with the company and ask the FBOs to sign a consent agreement to stop the disputed practices outlined in an accompanying complaint. If the FBOs follow the agreement, legal enforcement may not apply. In contrast, if the consent agreement cannot be achieved, the FTC may issue an administrative complaint which is much like a court trial starts before an administrative law judge by submitting evidences, hearing a testimony, and investigating the advertisements. In case of finding any non-compliance, the commission will decide suitable actions for further implementation. The final decision may be appealed to the U.S. Court of Appeals, and to the U.S. Supreme Court. The FBOs may also be liable to the consumer who affect health's problem resulting from that misleading advertisement.

For advertising dietary supplements, the FTC investigates complaints about false or misleading claims in relation with effectiveness of a wide variety of both domestic and imported supplements. During 1984 – 2003, there were around 120 cases regarding misleading supplement advertisements mainly related to deceptive claims with weight-loss, serious disease treatments like cancer, AIDS (FTC, 2003). In 2003, 6 out of 15 cases were in relation to misleading claims supplements with weight-loss which can be summarised as following table:

Table 10 Summary on legal enforcement of dietary supplement advertising cases in 2003

Problem	Enforcement action
Suspected false or unsubstantiated efficacy and safety claims for weight loss products containing ephedra, "Zymax" and "MillinexES," or St. John's wort, "Serotril," and unsubstantiated arthritis cure and other claims for a dietary supplement product containing glusosamine and chondroitin, "CartazyneDS."	- Civil penalties, injunctive and other relief.
Suspected false and unsubstantiated weight loss claims for "Berry Trim Plus" dietary supplement products containing Hydroxycitric Acid or "HCA" and ephedrine alkaloids from Ma Huang and unsubstantiated safety	- Order for a permanent injunction and monetary relief - Order requires payment of $195,000 in consumer compensation.

Problem	Enforcement action
claims for "Berry Trim Plus."	
Suspected false and unsubstantiated efficacy and safety claims for weight loss products, "Fat Sponge in a Pill" and "Calotrol/MD", one, "Meta-Biological" containing ephedra, and for a product for erectile dysfunction, "Virile V" containing androgen and yohimbe.	- Order for a permanent injunction and monetary relief - Order required payment of $175,000 in consumer compensation.
Suspected false and unsubstantiated disease treatment and cure claims and weight loss claims for "Seasilver" liquid supplement.	- Order for injunction and other justified relief - Inventories of Seasilver seized by the U.S. FDA
Suspected false and unsubstantiated claims that its dietary supplement, Cellasene™, would reduce or eliminate cellulite.	- Order for permanent injunction and settlement of claims for financial relief
Suspected false and unsubstantiated claims for a purported weight-loss product containing D-glucosamine.	- Order for permanent restriction and other Equitable relief and stipulated order for preliminary Injunction

In the same year, there was one case regarding unsubstantiated health claims for Physician's RX, a dietary supplement containing a variety of vitamins, minerals, and antioxidants. The company was legally ordered to pay for $215,000 civil penalty. According to reported cases, it may be assumed that the problems relating to advertising multi-nutrient supplements have still occurred but the level of public health impact is less than the deceptive claims on both weight-loss and disease treatments so that the FTC prioritised to legally enforce these problems prior to multi-nutrient supplements.

4.2.2.2 PREMISES PERSPECTIVE

Since major aims of enforcing the CGMPs for dietary supplements are to avoid wrong ingredients, too much or too little of a dietary substances, improper packaging and labelling, and contaminants to the products such as natural toxins, bacteria, pesticides, lead, all establishments must comply with this rule not later than three years after the final rule came into force as of June, 2008 (U. S. FDA, 2010). Therefore, the CGMPs rule was placed in all firms as of June 2010. After the completed enforcement of the CGMPs, it was reported that 55 facilities were inspected for the rule compliance and most of them conformed to the CGMPs (U. S. FDA, 2010). A study in 2006 (Crowley & FitzGerald, 2006)[176] also supported that even the one-time cost for equipment and facilities for the GMPs compliance may approximately over $ 54 million financially analysed by the U.S. FDA, most of dietary supplement industries welcome the CGMPs rule in order to separate the pretenders from the manufacturers who are spending the time and money to produce compliant and safe products as well as to improve total quality and consumer confidence in the industries. The financial impact of the CGMPs implementation may pass on to consumers resulting in increasing price of the dietary supplements, however, the same study addressed that most of US consumers support the government and industries to implement the CGMPs rule for better quality and safety aspects.

[176] Crowley and FitzGerald, 2006, p. 15

4.2.3 Communication and information exchange

After the Dietary Supplement and Nonprescription Drug Consumer Protection Act (U. S. FDA, 2006a) came into force on December 22, 2007, the FBOs must comply with the mandatory adverse event reporting for dietary supplements with following four major provisions[177]; 1) collect all adverse event reports by manufacturers, distributors, and retailers of the supplements; 2) legally submit the serious adverse event reports to the U.S. FDA within 15 working days of receipt; 3) maintain records of reports of all adverse events at the firms for 6 years and require that the U.S FDA be allowed to inspect those records; and 4) require dietary supplement labels to bear information for facilitating the report of serious adverse events associated with the use of supplement by consumers.

The adverse event means any health-related event associated with the use of a dietary supplement that is adverse, whereas the serious adverse event refers to an adverse event that[178]

(A) Result in death; a life-threatening experience; inpatient hospitalisation; a persistent or significant disability or incapacity; or a congenital anomaly or birth defect; or

(B) Requires, based on reasonable medical judgment, a medical or surgical intervention to prevent an outcome described under subparagraph (A).

Therefore, FBOs shall submit all serious adverse events to the U.S. FDA while mild and moderate adverse events are also reported on voluntary basis. The serious adverse event reports shall be submitted in a form of MedWatch 3500A which requires following information; an identifiable injured person; name of the person who first notified the responsible party; identity and contact information for the responsible party; a suspect dietary supplement; and a serious adverse event or fatal outcome.

In general, the report MedWatch 3500A form, along with a copy of the dietary supplement label and any other attachment are mailed to the CFSAN for serious adverse event reporting, however, the CAERS, a computerised system, has been developed since 2004 to collect and monitor all adverse event reports and product complaints that are related to CFSAN-regulated products. It also provides the CFSAN to organise, store, and review submitted adverse event report more efficiently and effectively by using electronic storage, coding and query software (Woo, 2007) leading to improve the post-marketing control of dietary supplement and facilitate the CFSAN's capability of trend analysis in the reporting of adverse events for this product. Consumers and health care providers may report adverse events on the voluntary basis and the U.S. FDA provides communication channels for reporting any adverse event such as FDA's MedWatch hotline at 1-800-FDA-1088 or report online available on the U.S. FDA website (U. S. FDA, 2012c). Similar to the domestic supplement, any imported product shall be rejected, if the U.S. FDA has credible evidence or information indicating that the responsible person has not complied with the new reporting requirements.

The GAO report of 2009 (GAO, 2009) indicated that 948 adverse event reports were submitted through the CAERS during January to October, 2008 which is a threefold increase comparing to over the same period in 2007 that was 298 received reports. A major reason of the increasing number is the mandatory reporting serious adverse event went into effect since December 22, 2007. From the 948 reports,

[177] Section 3 of the Dietary Supplement and Nonprescription Drug Consumer Protection Act
[178] Section 3 (a) of the Dietary Supplement and Nonprescription Drug Consumer Protection Act

596 were mandatory reported of serious adverse events submitted by the FBOs while the remaining 352 reports were collected from moderate and mild adverse events as well as the other serious adverse events voluntarily submitted by consumers and heath care providers. A list of suspected dietary supplements causing 596 serious adverse event reports was shown in the report as below table:

Table11 Number of cases with mandatory reported adverse event outcomes by dietary supplements product classification from December 22, 2007 to August 6, 2008[179]

Product classification	Number of serious adverse events	Percentage of all serious adverse events reported (%)
Combination product and products not elsewhere classified*	391	65.6
Vitamin	240	40.3
Mineral	111	18.6
Fats and lipid substances	55	9.2
Herbal and botanical (other than tea)	24	4.0
Fibre	20	3.4
Herbal and botanical tea	15	2.5
Protein	9	1.5
Animal by-product and extracts	1	0.2
Total	596**	

Remark: * This category refers to either combination products such as a product containing both vitamins and herbals, or a product which could not be categorised under one of the FDA's other product classification.

** Total does not add because some adverse events involved more than one product and are counted in more than one category. For example, if a consumer was taking both a Vitamin C supplement and an Echinacea supplement, the event would be classified under both "vitamin" and "herbal and botanical". If the consumer was taking a single product containing both Vitamin C and Echinacea, the event would be categorised under "combination products".

From the above table, it has been presented that micronutrient supplements causing serious adverse events are significantly reported while the trend of combination dietary supplements such as multi-vitamins and multi-minerals supplements continuously increases in the US market (Bailey et al., 2011; Timbo et al., 2006; Woo, 2007).

Apart from the adverse event reporting system, information on recall, market withdrawals, and safety alert of dietary supplements is also available on the U.S. FDA website (U. S. FDA) for both competent officers and consumers. Details of product such as brand name, name of company, including photo with the reason of problem are obviously provided. An example such of this information shows in below figure:

[179] GAO report of 2009, table 2

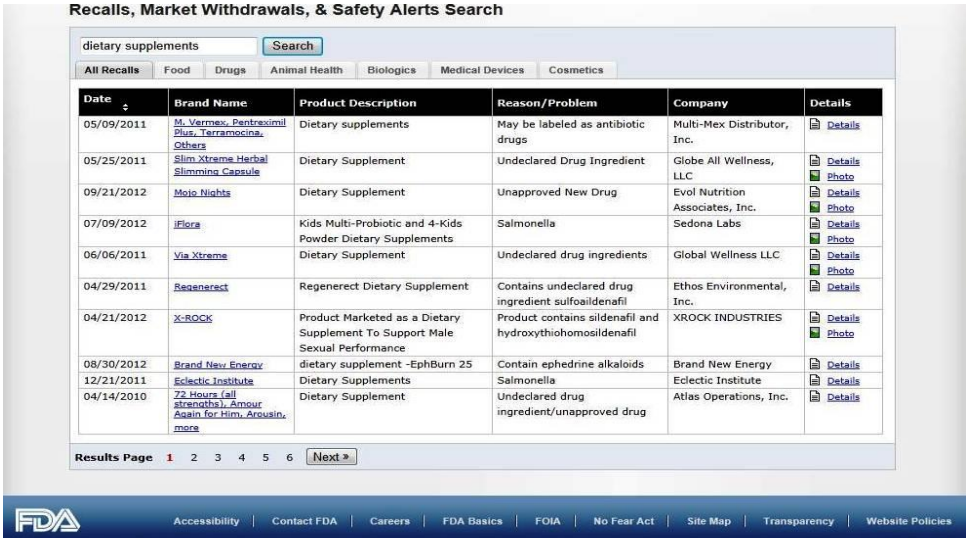


Figure 13 Information Recalls, Market Withdrawals, & Safety Alerts of dietary supplements[180]

In addition, monthly enforcement reports and annual warning letters are also regularly communicated to all stakeholders through this website.

4.2.4 Empowerment of competent officers, FBOs and consumers education

The U.S. FDA has developed guidance and guidelines relevant with regulations of dietary supplements. FDA's Compliance Programme Guidance Manual (CPGM) serves as work instructions to FDA personnel for conducting activities to evaluate industry compliance with the FD&C Act and other requirements. A specific compliance programme for imported and domestic dietary supplements has been developed and implemented since 2010. The Secretary of HHS also provide training and education programmes for all employees of state, local, territorial and tribal food safety officials relating to the regulatory responsibility and policy[181]. The programmes focus on scientific training, improving skill of inspection training, best practices training, administrative process and procedure and integrity issues, appropriate sampling and laboratory analysis methodology, and building enforcement action following inspection, examinations, testing, and investigations.

Moreover, many guidance documents are particularly provided for FBOs to comply with regulations related to dietary supplements covering 3Ps perspectives. For examples, draft guidance for new dietary ingredient notifications and related, guidance on CGMPs, a dietary supplement labelling guide, compliance guides for nutrient and health claims, including a guide for industry regarding the adverse events reporting; questions and answers in relation to adverse event reporting and recordkeeping for dietary supplements to comply with the Dietary Supplement and Nonprescription Drug Consumer Protection Act. All guidance documents are available on the U.S. FDA website[182], however, it has been clearly addressed that these documents are non-legal binding basis and they aim to facilitate and support FBOS for legal compliance,

[180] Website of U.S. FDA: Recalls, Market Withdrawals, & Safety Alerts Search: Dietary supplements
[181] Amended chapter X (21 U.S.C. 391 et seq. of the FD&C Act
[182] http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/DietarySupplements/default.htm

while the FDA officers may departs from these guidance as appropriate justification and supervisory concurrence (U. S. FDA, 2000)[183]. For advertising dietary supplements, the industry guide for advertisement and public communication is also disseminated by the FTC. In addition, the public workshop on Deception in Weight-Loss Advertising was arranged in 2002 for both competent inspectors and FBOs.

Information on dietary supplements for consumers is also provided through the U.S. FDA website in a concept of Questions and Answers which is user friendly while the publication entitled "Weight Loss: Finding a Weight Loss Program that Works for You" is available both hard copy and electronic file on the FTC website for consumers to self-evaluate the supplements.

4.2.5 Limitation and challenges on post-market control system

Even though a lot of information is available for both FBOs and consumers for regulatory compliance, problems on unauthorised ingredients in dietary supplements and misleading product labels including advertisements are still concerned as well as the product recall has been continuously reported by the U.S. FDA. According to the GAO report of 2009 (GAO, 2009), limitations of the U.S. FDA actions for enforcing the DSHEA and controlling dietary supplements were analysed. Firstly, ability of the U.S. FDA to identify the safety aspect of supplement is slowed down because lacking essential information in three major areas; 1) information on premises of dietary supplements which is incompletely available for the U.S. FDA; 2) information about products such as type, ingredients because of no pre-market approval for the dietary supplements before selling on the market; and 3) information about product safety such as adverse event reports because only the serious adverse event is legally submitted to the U.S. FDA, while mild and moderate adverse events are voluntarily reported which could be a beneficial scientific resource on the product safety and may support the U.S. FDA for safety-related conclusion.

Secondly, limitation of inspection resource leads to prioritise work according to public health risk and the dietary supplements are commonly considered as lower risk, comparing to other hazards such as foodborne pathogens. Due to this limitation, no foreign inspections of product establishments were inspected by the U.S. FDA during 2002-2008, meanwhile domestic premises were inspected approximately less than 1 percentage of total food premises in US. The next challenge for the U.S. FDA is to monitor FBOs to comply with CGMPs for dietary supplements because the final rule of CGMPs has just enforced since 2007 with full implementation in 2010 that is 16 years after the DSHEA came into force. Therefore, some establishments, especially in small and medium enterprises may have difficulty of compliance. Another problem is that the U.S. FDA lacks of authority to immediately remove unsafe product from the market because the U.S. FDA have to prove that the product is unsafe based on scientific evidence which is a time-consuming process. In addition, if any evidence shows that the product may harm to consumers, the U.S. FDA shall ask the HSS for permission before taking any action, while the voluntary recall depends on industry exercising its responsibility. The confusion of boundary products between dietary supplements and other special foods is one of limitations for the U.S. FDA to control product safety, especially in food containing added dietary ingredients which is not always clear for consumers. Complaints about misleading advertising dietary supplements have still increased in the US market, particularly in deceptive claims regarding weight-loss, disease treatments through worldwide commutation channels such as TV, Internet, and direct-sale market resulting in challenges both the FTC and the U.S. FDA to effectually conduct legal enforcement

[183] U.S. FDA, 2000, Code of Federal Regulations Title 21, Part 10 (subpart B-General Administrative procedures)

of the advertisements. The last challenge relates to consumers understanding on dietary supplements. Many studies revealed that consumers are not well-informed about safety, efficacy and labelling of dietary supplements and have obscurity interpreting labels on the products resulting in enhancing health risks associated with consuming these supplements. Moreover, currently the CFSAN has no on-going or new consumer education plan for dietary supplements due to resource limitation.

4.3 Thailand

Similar to other food products, dietary supplements sold to Thai consumers shall comply with the regulations and commonly monitored by the Thai FDA inspector . Activities of post-market control system in Thailand also concern on three aspects regarding the supplements; product, premises, and presentation. These measures are normally implemented to all supplement products on legal and voluntary basics. In case a non-compliant product is found, it will be immediately removed from the market whereas the FBOs shall be punished[184].

4.3.1 Inspection and sampling procedure

Thai FDA officers regularly inspect dietary supplements following the annual monitoring and surveillance programmes and the work instruction which is an internal quality document for competent officers to have a good practice on sample collection and preparation for analytical test. In addition, the sampling procedure was developed to guide inspectors the method of collecting food samples. For dietary supplements, the sampling procedure including law enforcement can be summarised as following table:

Table 12 Summary of sampling procedure and legal enforcement for dietary supplements placed on Thailand market

Step	Action	Responsible person
1. Sampling	- each sample will be collected about 50 tables or 100 g, depend on product characterisation - In case the numbers of sample in the same lot are insufficient, other lots mostly related to the sample may be collected.	An authorised officer
2. Sample preparation	- Mark and seal all samples in such a manner as its nature. - Fill the sampling form with necessary information such as sample detail, purpose of sampling, and require the FBOs to sign in this documents (if necessary) - Provide one copy of signed document to the FBOs	An authorised officer by coordinating with FBOs
3. Sample distribution	- Send all samples to an official laboratory, DMSc. - Record the information of sample submission	An authorised officer
4. Sample analysis	- Analyse the received sample according to legal requirements. - Submit the result of analysis to the competent authority, the Thai FDA	An approved examiner

[184] Chapter 7 and chapter 8 of the Food Act B.E. 2522 (1979)

Step	Action	Responsible person
5. Result of analysis 5.1 Compliance	- Record the compliant products and keep monitoring.	An authorised officer
5.2 Non-compliance	- Recheck the suspected products by collecting more samples in case of sampling at the sellers. - Recheck the establishments based on GMP requirements.	An authorised officer
	- If the analytical result confirms this non-compliance, and/or the premises is not complied with the GMP requirements, punishment and/or suspension of premises licence shall be applied.	An authorised officer
	- Write the report of non-compliance and send its copy to the FBOs	An authorised officer
	- Submit the results to the Food Committee for consideration on any measure such as punishment, withdrawal and/or recall as appropriate	An authorised officer
	- Discuss and provide the suitable measures for consumer health protection	the Food Committee by coordinating with the FBOs
	- Implement the preventive measures approved by the Food Committee such as reject, withdraw, recall, or destroy the suspected products.	An authorised officer
6. Punishment*	a person who is guilty of an offence shall be liable; - To imprisonment of not more than 2 years and a fine of not more than twenty thousand bath** (approximately € 500) or both, in case of impure product, e.g. contamination of pathogen. - To imprisonment from six months to the years and a fine from five thousand baht to one hundred thousand baht (around €125 – 2,500), in case of adulterated products, e.g. misleading label, defrauding premises registration number, or the result of quality analysis is less or exceed 30% of the requirements. - To fine of not more than fifty thousand baht (around € 1,250) or both, in case of substandard product which its analytical result has exceed the requirements but not exceed 30% of the legal limit. - To imprisonment of not more than five years and a fine of not more than fifty thousand baht (around € 1,250) or both, in case of non-complaint product which specified by the Minister, e.g. urgent hazards - To fine of not more than thirty thousand baht (about €750), in case of non-compliance of product labelling and, labelling criteria, and advertisement on the labels.	An authorised officer

Remark: * based on chapter 7 and chapter 8 of the Food Act B.E. 2522 (1979).
** Exchange currency rate is approximately € 1 = 40 baht.

Similar to domestic supplements, samples from imported products and their labels are collected at the port of entry following the annual monitoring plan, specific issues ordered by the Thai FDA, and suspected cases related to safety issue. Documents in relation to the product are regularly checked for compliance with the pre-market approval while the sampled products will be sent to the reference laboratories. The products will be released from the port of entry in case that they are complied with all requirements, otherwise, non-compliance supplements will be either rejected or destroyed (Tippayakunanon, 1996)[185]. In addition, the punishment provision of imported supplements is as same as domestic products.

4.3.2 Monitoring and Surveillance programmes

The Bureau of Food under the Thai FDA has a main responsibility to develop monitoring and surveillance plan for legal compliance. This plan is annually reviewed and revised based on current situation in relation to food products focusing on 56 categories of the notifications of MoPH. In addition, a principle of FAO/WHO on application of risk analysis to food standard issues, survey data from central and local areas, results from surveillance, including consumer complaints are also taken into account of developing monitoring and surveillance programmes. Dietary supplements classified as one of food products are also monitored and enforced by law following this plan.

4.3.2.1 PRODUCT AND PRESENTATION PERSPECTIVES

Three monitoring and surveillance programmes regularly implement for controlling all food products including dietary supplements in the Thailand market:

1) A regular plan in order to monitor product in ordinary conditions;

2) An additional plan based on the policy to conduct some interesting products following the minister policy; and

3) A special plan for any hot issue regarding incident or emergency problem and to provide proactive measures.

A sampling plan for each type of the monitoring and surveillance plan is statistically established by considering relevant regulations, scientific data from pre-market approval, and survey results. There are 5 steps for developing the sampling plan which are summarised as following figure:

[185] Tippayakunanon N., 1996.

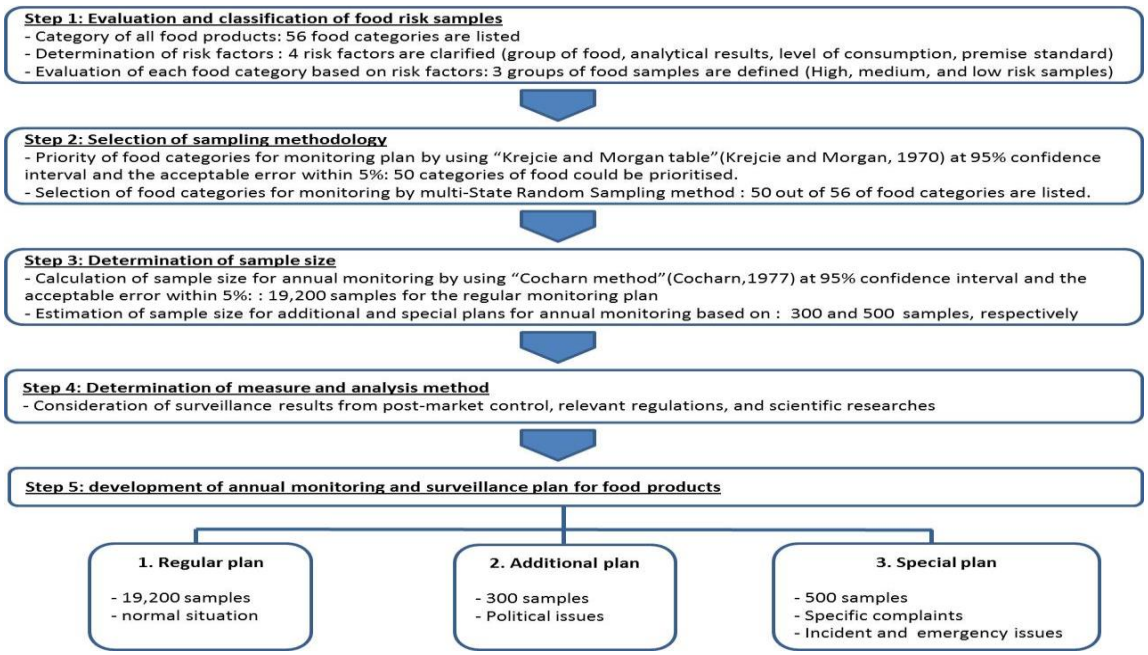


Figure 14 Development of monitoring and surveillance plans for food products (T. FDA, 2010)

In a total of 20,000 samples taken from the annual monitoring plan, 50 samples or 0.25% are estimated for monitoring dietary supplements. The samples are normally collected from the manufacturers and markets before sending to the laboratory unit to analyse and check for legal compliance. During 2009-2011, results of monitoring dietary supplements were present as following table:

Table 13 Result of monitoring dietary supplements sold in Thailand during 2009-2011

Year	Number of samples	Number of compliant samples	Number of non-compliant samples	Percentage of non-compliant products
2009	86	80	6	6.98
2011	97	89	8	8.25
2012	74	65	9	12.16
Total	257	234	23	8.95

According to the annual report of analytical results in Food of 2011 (T. FDA, 2012a), food products such as meat products, honeys, fruits and vegetables, drinking water in the sealed containers, food additives, daily products, were highly concerned for monitoring activities, comparing to the dietary supplements which often affect medium risk to human health. However, most of non-compliant dietary supplements related to adulteration with drug substances such as Sibutramine, Sidenafil, Phenolpthaein, and Dexamethansone for weight loss, whereas problems on unauthorised multi-micronutrients and botanical substances contained in the supplement products are still found. Imported supplements have regularly checked at the port of entry, and unpermitted heavy metals such as Arsenic (As), Cadmium (Cd), Lead (Pb), Mercury (Hg) are often found. Enforcement measures will immediately apply if there is any scientific evidence or analytical result that confirms the non-compliance.

For advertising dietary supplements, they are normally inspected and monitored on the legal basis. In case of misleading advertisements[186], the advertiser or responsible person shall be punished by imprisonment of not more than three years and a fine of not more than thirty thousand baht (around € 750) or both[187]. Unauthorised advertisement or other presentations relating to dietary supplements shall be prohibited and the advertiser or a guilty person shall be fined by less than five thousand baht (approximately € 125). In addition, the competent authority may issue a warning letter requiring the FBOs to either restrain the unauthorised advertisement or stop the production or importation of the suspected supplements[188]. Any FBOs who is not complied with the letter, he shall be punished by imprisonment of not more than 2 years or a fine of not more than twenty thousand baht (around €500), or both[189].

The study on pattern and media used for advertising dietary supplements in Thailand (Tiasuwan, 1999) revealed that all of public media are used for advertising supplements such as TV, radio, newspaper & magazine, other printing materials like catalogue, brochure, poster, and other media channels, e.g. internet and direct selling. From this study, the advertisements from TV and radio were mostly complied with the requirements because they could be easily inspected, comparing to others such as newspaper and magazines which often advertise the supplements by using reference person or experts giving technical article in relation to the products, but the fact of health impact from product usage always be hidden from the advertisement. Similar to newspaper and magazine, other printing materials mostly present technical information to support advantages of food supplements and they are widely distributed from the shops. Therefore, the competent inspectors have to collect these printing materials for monitoring the compliance. Advertising supplements through internet and direct sale has significantly increased and they are mostly difficult to control because the information is always changed while the source of information is too hard to trace back. To avoid misleading advertisement in long-term period, consumer education is necessary. The study on advertising food by direct sale system (Kampopong, 2004) clearly presented that the advertising dietary supplement is the most problem found from monitoring survey and consumer compliant while the direct selling is a major source of misleading advertisements.

Similar to the product perspective, unauthorised advertisements of dietary supplements and unproven claims are frequently found based on the monitoring and survey throughout all public media, particularly in weight-loss claims. An example of enforcement results in September, 2011presented that 17 out of 46 cases were associated with dietary supplements and mostly found illegal presentation through public media as a following table:

Table 14 Result of legal punishment regarding non-compliant food supplements in September, 2011(T. FDA, 2011c)

Product	Guilty person	Illegal issue	Enforcement action
Dietary supplement "Power 3"	Producer	Unproven claims for a purported weight-loss product	Fine for 20,000 Baht
	ViVi Magazine editor		Fine for 2,000 Baht

[186] Section 40 of the Food Act B.E. 2522 (1979)
[187] Section 70 of the Food Act B.E. 2522 (1979)
[188] Section 42 of the Food Act B.E. 2522 (1979)
[189] Section 72 of the Food Act B.E. 2522(1979)

Product	Guilty person	Illegal issue	Enforcement action
	Cawai Magazine editor		Fine for 5,000 Baht
Dietary supplement	OHO Magazine editor	Unauthorised advertisement	Fine for 5,000 Baht
Dietary supplements	Seller	Unproven claims for a purported weight-loss, disease treatment product	Fine for 1,000 Baht
Dietary supplement "Silky Colla"	Producer	Unauthorised advertisement relating to treat or cure human disease	Fine for 2,000 Baht
Dietary supplement "ASA"	OHO Magazine editor	Unproven claims	Fine for 5,000 Baht
Dietary supplement "Gluta MC Claire", "Gluta MC Tim", and "Creatine Plus"	Seller	Unproven claims	Fine for 4,000 Baht
Dietary supplement "Citrink"	Cable TV	Unproven claims	Fine for 2,000 Baht
Dietary supplement "Lifetech Fibery"	Chee-Vit-Jing Magazine editor	Unproven claims	Fine for 5,000 Baht
Dietary supplement "B5"		Unproven claims	Fine for 5,000 Baht
Dietary supplement "Kara Plus"		Unproven claims	Fine for 5,000 Baht
Dietary supplement "Bright Up"	Poo-Ying Magazine editor	Unproven claims	Fine for 4,000 Baht
Dietary supplement "Creatine Plus"	Oops! Magazine editor	Unproven claims for a purported weight-loss product	Fine for 5,000 Baht
Dietary supplement "Gano SP" containing lingzhi mushroom extract	Producer	Misleading labelling and unauthorised advertisements	Fine for 6,000 Baht

4.3.2.2 PREMISES PERSPECTIVE

Establishment of dietary supplements is commonly inspected every 3 years for GMP compliance, similar to other food products. In addition, the premises shall be strictly investigated in case the non-complaint product is found by the competent inspectors. If any scientific evidence shows that the premises does not comply with the GMP requirements, the FBOs shall be fined of not more than ten thousand baht (about €250) and may, moreover, the premises licence shall be suspended or revoked if result of the tests on the dietary supplement is found to be either impure, adulterated, or substandard product on case-by-

case basis[190]. The Thai FDA annual report of 2011(T. FDA, 2011a) showed that 98.76% of establishment in Thailand were complied with the GMP provision which increased from 97.89% in 2010. However, number of establishment for dietary supplements was not specified.

4.3.3 Communication and information exchange

In Thailand, there are two major communication tools for information exchange regarding dietary supplements:

1) Reporting adverse product reactions from all health products such as drug, cosmetic, and food including dietary supplements. The reporting system connects between all public hospitals and the Health Product Vigilance Centre (HPVC) of the Thai FDA (T. FDA). Any adverse effecting consumer health resulting from medication error or product defect will be reported by a contact person through either written form or online submission. After collecting all data, the HPVC will evaluate the reports based on an epidemiological principle and a statistical database, and then will report to the Committee and the Secretary-General of the Thai FDA in order to provide appropriate measures for consumer protection. In addition, this reporting system has also connected to the WHO international Drug Monitoring Programme since 1984 to exchange public health information among international organisation and other member countries for strengthening an effectiveness of the surveillance system. However, most of reports associate with drug abuses, comparing to the dietary supplements. For an example, the monthly report of September 2012 (T. FDA, 2012b) indicated that 5,975 reports collected from all public hospitals and producers were related to adverse effect from drugs, however, only 1 report on dietary supplements with low health effect was issued.

2) Consumer complaints in relation to health products including dietary supplements throughout many communication tools provided by the Thai FDA such as hotline (1556), electronic mail, and letters. All complaints will be initiatively considered and then sent to competent officers of each product for further investigation and law enforcement, in case of non-compliance. The highest number of consumer complaints is from food products, while the complaints related to dietary supplements constantly increase. During 2010 - 2012, dietary supplements were one of top ten products which are mostly complained by the consumers. The numbers of consumer complaints in relation to the supplements were concluded as following tables;

Table 15 Number of consumer complaints for dietary supplements during 2010-2012 (T. FDA, 2012c)[191]

Year	Number of complaints regarding food products	Number of complaints regarding dietary supplements	Percentage of complaints regarding dietary supplements
2010	624	37	5.9%
2011	644	43	6.7%
2012	586	39	6.6%

According to the above table, main reasons of complaints are 1) adulterated product and 2) unregistered product, but the category of dietary supplements of the complaints was not specified.

[190] Chapter 7 of the Food Act B.E. 2522 (1979)
[191] Thai FDA. Budget annual report 2010-2012.

4.3.4 Empowerment of competent officers, FBOs and consumers education

Even the surveillance programme on dietary supplement is voluntarily implemented by the provincial health offices; the Thai FDA may collaborate with the provincial health officers to recheck the suspected product and its premises on case-by-case basis. In addition, if there is any doubted supplement sold in the area, the provincial health officer can also send the product and its information to the Thai FDA for further analysis and legal enforcement. Therefore, many guidelines, training programmes and meetings are often arranged to the competent officers both central and provincial levels in order to strengthen effective skill for monitoring and enforcing food regulations. All activities for empowering competent officers at the provincial areas will be constructed by the Rural and Local Consumer Health Products Promotion Protection Division that closely collaborates with the Bureau of Food, in case of all food products including dietary supplements, while the central competent officers are regularly trained by international agencies such as FAO, WHO, ILSI, and ASEAN. All work instructions and data of surveillance are provided for all competent officers under intra-network system of The Thai FDA.

Guidelines on dietary supplements for FBOs are available on the website of the Bureau of food as well as the one-stop service centre (OSSC) serves as a rapid service hub for all FBOs to apply the pre-market authorisation of dietary supplements. All necessary forms and list of information are available on the website of the OSSC[192].

Apart from officers and FBOs, consumer education is necessary for self-prevention from unsafe dietary supplements. The Public and Consumer Affair Division is a major responsible agency to publish education materials and disseminate to all public media. Knowledge of understanding product claims, dietary supplements choice, and hazards from misuse of product is transferred to user friendly information such as animation, theatre, radio, news, and print media like E-magazine, poster, brochures which are also available on the website[193]. In addition, the specific information for dietary supplements is also served by the Bureau of Food to educate consumers such as "how to choose an appropriate dietary supplement for consumption", which is free download on the website[194].

4.3.5 Limitation and challenges on post-market control system

Several limitations of post-market control for dietary supplement in Thailand are proposed. An example of the study in 1996 (Tippayakunanon, 1996) analysed restrictions of import control system for dietary supplements as follows;

1) Information system is less effective and lack of well-connection among competent agencies resulting in time-consuming for data collection and late response for consumer protection. In addition, scientific researches on dietary supplements are less updated leading to less proactive measures in case of an incident or emergency problem.

[192] http://newsser.fda.moph.go.th/ossc/tha/frontend/index.php
[193] http://www.oryor.com/oryor/pub_emag_main.php
[194] http://iodinethailand.fda.moph.go.th/food_54/data/document/2554/CS01.pdf

2) Lack of well-integration with other relevant agencies such as the Custom Department who takes main responsibilities of controlling all imported products. In addition, the traceability system is not mandated for all stages of the supply chain, unlike the EU system, so that preventive measures are often delayed.

3) FBOs are lack of responsibility, especially in suspected supplements. Controlling measures are mostly provided by the competent authorities while the FBOs are less willing to cooperate with the officers. It may be assumed that the legal requirement of the responsibilities is not addressed in the Food Act B.E. 2522 (1979), comparing to the GFL of EU, resulting in difficulties for competent officers to efficiently control and monitor the product.

4) Consumers are less educated, especially who live in rural areas.

Not only above limitations affecting post-market control of both imported and domestic supplements, but also problems of budget and human resource restrictions for sampling and analysis. Priority of food products for sampling is necessary and from the surveillance database, the supplement is not defined in the high risk group of food products.

4.4 Summary

In a brief summary, a major difficulty on this chapter is about limitation of accessible information, however, according to available resources; it has been shown that the post-market system is essential for safety and quality controls to all food products including food supplements. All of three regions have placed the post-market control system for food supplements on both voluntary and compulsory basics. The effective system needs close collaboration between competent inspectors, laboratory examiners, FBOs, and consumers. In addition, a systematic and practical procedure of sampling and rapid communication system can support competent officers to work professionally.

In author's point of view from comparing three different countries, the post-market control system in Ireland is the most well-organised mechanism for food supplements, while key factors influencing this achievement are 1) the submission for pre-market assessment both product and label elements, 2) the Integrated monitoring plan at national level, 3) the active intra- and inter-network systems, and 4) FBOs responsibility and the traceability system under the GFL . Comprehensive and scientific information can support relevant authorities to develop effective monitoring and surveillance plan as well as to provide proactive measures for consumer protection, in case of non-compliance. In contrast, the post-market system for dietary supplement in US is mostly challenge for all officers due to lack of scientific evidence and necessary information regarding the supplements. For Thailand, the post-market system is likely similar to US, particularly in responsible of the competent authority for burden of proof from non-compliant products. Unlike Ireland, Thailand has less effectiveness of post-market control due to lack of updated information of supplements, lack of an integrated monitoring plan among competent authorities, less active communication network with all stakeholders. In addition, lack of legal traceability leads to time-consuming response for investigating suspected product and taking any proactive measure. It has been also present that although the risk from food supplements is classified as a middle level and priority of post-market control is not highly concerned in some countries, problem on micronutrient supplements yet occurs in the market, especially in multi-vitamins and multi-minerals, whereas problem on botanical supplements has continuously increased because of consumer perception and history of use. Consumer education is significantly concerned by all of three countries because it is an essential measure for long-term prevention.

5. COMPARISON

Previous chapters present that food supplements are safely controlled by three perspectives, while many agencies and measures are involved in the control systems of EU, US, and Thailand in order to protect consumer health, provide reliable information for consumer choice, and facilitate the fair trade. Since EU, US, and Thailand are members of WTO, the codex guidelines on vitamin and mineral supplements adopted by the CAC in 2005 support the WTO members to enact their regulations in order that the national rules are conformed or harmonised to the international recommendation as well as any SPS measure relating to food supplements is in line with the WTO and SPS agreements.

Even the codex guidelines and risk analysis principle are referred for providing the measures in three countries, not all measures are similar depending on individual scientific evidences, national consumption data, monitoring and surveillance plan, consumer perception, risks from other relevant food products, production technology, and impacts on social and political issues in relation to the supplements. Therefore, differences and similarities of the regulatory systems between Codex guidelines and national regulations of EU, US, and Thailand regarding food supplements as well as comparison on control measures among three different countries are questionable.

In this chapter, comparisons of regulatory systems of food supplements from EU, US, and Thailand will elucidate with different aspects such as organisations, regulations, and measures of both pre- and post-market control systems on food supplements. According to the aspect of regulations, the codex guidelines concerning on three perspectives of supplements are also analysed for comparison with the national requirements in these three countries.

5.1 Aspect of organisations

All three countries indicate major competent authorities working for legislating, enforcing and improving these requirements to approach the ultimate target. In addition, these main authorities also participate in international meetings likes the CAC and sub-committees in order to develop international guidelines related to the supplements. Even the Codex guidelines are not fully adopted, all WTO members including EU, US, and Thailand take consideration on these guidelines for adapting into national rules based on availability of scientific evidence. It has been shown that the national and/or regional scientific information is an essential element in all three countries for developing regulations, and measures of pre-, and post-market controls, especially in the evaluation of a new substance. The principle of risk analysis (FAO/WHO, 2006a)[195] consisting of risk assessment, risk management, and risk communication is also a conceptual framework to develop laws and relevant measures in these three countries. From two principal aspects, these regulations not only comply with the WTO and SPS agreements for consumer protection, but also support trade facilitation regarding food supplements.

On the other hand, according to relevant laws, a managerial system is significantly different among three countries. In EU, every food regulation shall be comprehensively considered for effective implementation in all MSs. The GFL acts as a fundamental law for all food commodities, while the EC Directive 2002/46/EC for micronutrient supplements was incorporated into the national law with full

[195] Section 1.2 Risk analysis, p.5

compliance by July 2005. Therefore, main requirements such as a positive list of allowed micronutrients, pre-market authorisation of new substance, the GMP system, labelling and claims shall comply with the directive and relevant mentioned regulations but some specific technical requirements and enforcement measures, especially in post-market control may differ among MSs, such as maximum or minimal levels of certain micronutrients or notification of new food supplements (CBI, 2012b)[196]. However, the national requirement shall be submitted to the EC for further endorsement. Unlike US and Thailand, the independent risk assessment body as EFSA plays an important role to support the EC for decision making on regulatory revisions and proactive measures to control food supplements.

Comparing to the EU system, the relevant laws of both US and Thailand directly apply to all states or provinces, as well as post-market control system which is a unique enforcement. In addition, a central authority likes the U.S. FDA and the Thai FDA are mainly responsible for regulating and enforcing requirements related to micronutrient supplements for compliance. The U.S. FDA has a collaborative partner as the FTC to support monitoring compliance of advertisements, whereas the Thai FDA handles all activities about food supplements from regulating notifications, pre-market authorisation, to post-market enforcement because of resource limitation that may lead to confront a risk on conflict of interest, late response on pre-market authorisation, less update on rule revisions, and delay actions for post-market activities, in case of non-compliance. In addition, a provision on traceability system is still based on voluntary principle leading to have a less effective system than the EU. A summary of organisational comparison among three countries is described in below table:

Table 16 Summary of comparison on an organisation perspective in EU, US, and Thailand.

Item	EU	US	Thailand
Major laws of food supplements	- Regulation EC 178/2002 - Directive EC/46/2002 - National laws	- DSHEA Act of 1994 - FD&C Act of 1938	- Food Act B.E. 2522 (1979) - Notification of MoPH No. 293 (2005)
Principle of risk analysis	√	√	√
Risk Assessor	EFSA	The commission of Dietary Supplement labels, and the ODS	Sub-committees
Risk Manager	EC and MSs	HHS	Food Commission
Risk Communication tools	- RASFF at EU level - Safety Net at national level in Ireland - Consumer complaint system	- Adverse event reporting system - Consumer complaint system	- Adverse event reporting system - Consumer complaint system
Responsible agency for law	- European Commission at	- U.S. FDA at federal level for product,	- Thai FDA at national level

[196] Since the establishment of maximum and minimum level of vitamins and minerals is not yet approved by the EC, national level can be set up.

Item	EU	US	Thailand
enforcement	regional level - Food safety authority at a national level	premises, presentation - FTC for product advertisement	
Member of WTO and CAC	√	√	√
Requirement on scientific evidences	√	√	√
Ultimate goals	Consumer protection, truthful information of product for consumer choice, and trade facilitation		

5.2 Aspect of regulations and relevant requirements

According to the EC directive, DSHEA act, and notification of the MoPH on dietary supplements, they concern on consumer safety, efficiency and right of choice but the ways of protection are different. In US, the DSHEA was enacted based on industrial-friendly concept so that the safety and efficacy of certain supplements are not required by the U.S. FDA, except a new ingredient which is required to submit scientific data through the pre-notification procedure. The EU and Thailand take a different approach by providing a positive list of allowed micronutrients after their safety and bioavailability are assessed. In case any ingredient is not in the list, pre-market authorisation is required before that food supplements are sold on the market, while a "develop first, ask question later" approach applies in US (S. A. Mason, 2010)[197].

Under the Codex guidelines for vitamin and mineral food supplements (CAC/GL 55-2005) (Codex, 2012b), a food supplement is classified as food and it may influent to the classification of this product in EU, US, and Thailand which also categorise the supplement as food for the international compliance. However, the scope of food supplement in the Codex guidelines is narrower than the national regulations in EU, US, and Thailand because only the micronutrient supplement is specified in the Codex standards, while more substances are included in the three national regulations and revised provisions such as amino acid, fatty acid, and botanical ingredients. According to the scope of food supplement, scientific resources, and other factors, some technical requirements are far different among these three countries as well as the Codex guidelines. Hence, similarities and differences on regulations in relation to the supplements are analysed by three perspectives (3Ps); Product, Premises, and Presentation.

5.2.1 Product Perspective

It has been explained in the chapter 3 that the definitions of food supplements, particularly in vitamins and minerals from three different countries are mostly similar to the Codex guidelines. The scope of both international standard and national regulations excludes medicinal products, and foods for special dietary uses in order to avoid consumers from confusion of these products.

[197] Section III (B), p. 118.

Even a positive list is not required in the Codex standards, it states that selection of vitamin and mineral should be based on consideration such as their safety and bioavailability by taking into account either FAO/WHO standards, recognised international standard, or national legislation[198]. According to this statement, EU and Thailand has adapted into legal requirements by developing a positive list of permitted types and forms of micronutrients for food supplements on risk assessment basis including the maximum limit of each micronutrient, especially in the Thai regulations. FBOs who would like to produce the supplements containing permitted micronutrients are not required for pre-market authorisation, while a product consisting of any new substance excluded from the list shall be pre-authorised by the competent authorities before they are sold on the market. Moreover, in EU, the positive list is necessary to implement because national rules of food supplements may differ among MSs resulting in obstruction of the free movement, creation of unequal trade competition, and impact on the functioning of the internal market. Comparing to EU, a major purpose of the positive list applied in Thailand is likely to have a more effective measure for controlling these products before reaching consumers rather than to facilitate trade. Unlike EU and Thailand, a positive list is not legally required under the DSHEA due to facilitate manufactures and provide more freedom of consumer choice (Miller, 2008). Under this Act, the old substances which have been marketed before October 15, 1994 can be directly applied into supplements without document submission. On the other hand, a new substance which generally presents in food supply or evidently shows history of use can be used in the supplements after 75 days notifying to the U.S. FDA. FBOs have to support scientific information for the new substance and it will be published after 90 days following its receipt. From author's point of view, the pre-market notification of the new substance in US has significantly different intention with the systems in EU and Thailand. The systems in EU and Thailand focus on risk assessment to ensure that the allowed ingredients are safe for human consumption leading to require a lot of scientific documents, have a complicate process, and consume time of application. However, the pre-market notification in US may focus on a more transparency process for consumers but the new substances are not guaranteed for safety and efficiency on legal basis.

The Codex guidelines indicate that the minimum level of each vitamin and/or mineral contained in a supplement per daily portion of consumption should be 15% of the recommended daily intake proposed by the FAO/WHO[199]. EU and Thailand by considering this international standard, adopted this number into national rules under the Council Directive 90/496/EEC on nutrition labelling for foodstuffs[200] and the Notification of MoPH no. 293 B.E. 2548 (2005)[201], respectively. For the maximum level, the food supplement directive of EU is significantly harmonised with the concept in the codex standard[202]. Both upper safe levels of micronutrients based on risk assessment and the daily intake from other foods sources are taken into account for establishing maximum level of each substance contained in food supplements. It has been presented in the EU that the process of this development is time-consuming after the directive has been enacted since 2002, and the ULs for 34 nutrients were published in 2006 while the maximum levels are now still in process of discussion by the EC. Comparing to Codex and EU concepts, the Thai FDA have established

198 Section 3.1.2 of the CAC/GL 55-2005
199 Section 3.2.1 of the CAC/GL 55-2005
200 The Council Directive 90/496/EEC, Annex I. To declare micronutrients in nutrition labelling, their amount is calculated per 100 g or 100 ml or one package.
201 Notification of Ministry of Public Health (No.293) B.E. 2548 (2008), clause 5(5) for allowed vitamins and minerals in the positive list.
202 Section 3.2.2 of the EC Directive 2002/46/EC

the maximum level of micronutrients in the positive list based on the Thai RDI principle. The upper safe level of intake is mainly considered but the amount of micronutrients from other food sources is not yet taken into account resulting in overdose consumption and may affect to consumer health. In contrast, neither minimum nor maximum level of micronutrients is mandatory set up under the DSHEA of US. The safety level of micronutrients in the supplements shall be assured by the FBOs while the scientific information regarding on safety and efficiency is not required by law. Therefore, it is an obstacle for a competent agency like the U.S. FDA to prove this evidence after the product is placed on the market.

Another requirement regarding safety aspects is also included in the Codex guidelines for micronutrient supplements such as packaging[203] which generally applies for all foods. There is also no specific requirement for packaging of food supplements in EU, US, and Thailand, while other safety aspects are addressed in the national and regional regulations of supplements much more than in the Codex guidelines, such as pathogens, food additives, and contaminants which are concluded in the chapter 3 of this thesis.

5.2.2 Premises perspective

A food hygiene principle is not stated under the codex guidelines on vitamin and mineral supplements, however the Codex food hygiene guidelines (CAC/RCP 1-1996) are recommended to apply in all food establishments that mean it also covers food supplements. The general principle of food hygiene (CAC/RCP 1-1996) was revised as the fourth revision (CAC/RCP 1-1969, Rev. 4-2003) (Codex, 2003) which includes annex on HACCP system and general guideline for its application. It was adopted by the CAC in 1997 and revised in 2003 before circulating to all codex members[204]. Under the objectives of these guidelines[205], the food hygiene principle is recommended to apply based on from farm to fork approach to ensure that food is safe and suitable for human consumption, whereas the HACCP-based system is suggested as a means to enhance food safety. All regulations of food supplements of EU, US, and Thailand adapted these guidelines into national requirements for controlling the food supplements with different approaches. In EU and Thailand, the regulations of food hygiene were developed to apply for all kinds of food products that are not specific for food supplements. By comparing between EU and Thailand, the EC regulation on food hygiene (EC Regulation 852/2004) clearly addresses[206] that this requirement shall apply throughout the food chain, starting with primary production based on the HACCP principles, together with the good hygiene practice, while the primary production and HACCP system are not indicated in the notification of MoPH No.193 B.E. 2543 (2000) since capabilities both human and budget resources of the FBOs in Thailand, especially in small and medium enterprises are limited to comply with the system in a short-term period. Therefore, the GMP based system legally applies in all food premises including dietary supplements in Thailand as a minimal requirement. However, the GMP system for dietary supplements has been developed based on Codex standard and ASEAN Traditional medicine and health supplement good manufacturing practices (TMHS GMP)[207] in order to improve quality system of supplement production as well to harmonise the good practices among 10 ASEAN member countries under the ASEAN Economic Community (AEC) agreement which is fully implemented in 2015 (Intarapanich P., 2012).

[203] Section 4 of the CAC/GL 55-2005
[204] The Recommended international code of practice general practice of food hygiene (CAC/RCP 1-1969, Rev. 4-2003)
[205] Section I of the CAC/RCP 1-1969, Rev. 4-2003
[206] Item 1(d) of the article 1 of the Regulation (EC) No. 852/2004
[207] In ASEAN, a heath supplement is an official word for food supplements and dietary supplements.

Unlike EU and Thailand, the good practice for dietary supplements was specifically established in US. The final rule of CGMPs was established in 2007 and fully enforced in 2008 to all levels of enterprises involved in producing, packing, and distributing the supplements sold in US. According to the CGMPs rule, it likely combines between GMP and HACCP systems because not only fundamental requirements of GMP are addressed such as design and facilities of establishment, operation control, maintenance and sanitation, personal hygiene, but also some specific criteria based on HACCP approach are mentioned, e.g. quality control procedure, material and final product testing, and record keeping. A more specific requirement in CGMPs provision is the identity testing of dietary ingredients, except the FBOs who apply for 100% identity testing exemption proposed in the Interim Final Rule (IFR) provision. The exemption is on case-by-case basis and decided by considering sufficiently scientific information, while a certificate of analysis for specification other than the identity of its ingredient from a competent supplier is an option instead of having manufacturers conduct tests or examinations on the components (U. S. FDA, 2007)[208]. In addition, a management of returned dietary supplement and product complaints are also indicated in subpart N and subpart O of this provision (U. S. FDA, 2007) in order to require FBOs having a systematic procedure with record maintenance to assess suspected supplements and protect consumer health in a timely manner. These additional subparts and the requirement of record keeping in every step significantly support competent authorities and consumers to deal with unsafe supplements when the restriction of product obligation is soft.

5.2.3. Presentation perspective

There are two codex standards recommended for products' presentation[209]; the Codex Standard for the Labelling of Prepackaged Foods (Codex-Stan 1-1985, Rev. 1-1991), and the General Guidelines on Claims (CAC/GL 1-1979, Rev. 1-1991). Moreover, specific recommendations for supplement labelling are also addressed such as indication of "food supplement" term, declaration of micronutrients amount in numerical form with per portion of the product as recommended for daily consumption or per unit for single use, percentage of the Nutrient Reference Values (NRVs), information of usage, nutrition labelling in case any nutrition or health claim is declared, including clear warning statements to avoid replacement of meals or a varied diet, exceeding consumption and product accessibility by young children. Comparing to the codex provisions, labelling requirements for food supplements of EU, US, and Thailand are significantly conformed. Apart from this essential information needed to present on the product label, US and Thailand also regulated more specific requirements such as font size, background colour. A supplement fact is required in US, whereas declarations of food serial number and other additional ingredients such as food additives are mandated in Thailand. A main purpose of both principle and additional requirements on supplement label is to provide reliable information for consumers while more additional requirements on product information may differ from country by country depending on consumer perception, experience, and expectation (M. J. Mason, Scammon, & Fang, 2007).

According to the codex general guideline on claims (FAO/WHO, 1979)[210], a claim is "any representation which states or implies that a food has particular characteristics relating to its origin, nutritional properties, nature, production, processing, composition or any other quality". There are five claims should be prohibited; 1) claims providing an adequate source of all essential nutrients, except in case

[208] The CGMPs for dietary supplements, section B. Highlights of the Final Rule, P. 34765
[209] Section 5 of the CAC/GL 55-2005
[210] Codex General Guidelines on Claims (CAC/GL 1-1979, Rev. 1-1991)

of well-defined products by codex standard or accepted by the authorities; 2) claims implying that a balanced diet or ordinary food cannot supply adequate amounts of all nutrients; 3) claims which cannot be substantiated; 4) claims referring to the prevention, alleviation, treatment or cure of disease, disorder, or particular physiological condition, unless they are classified as foods for special dietary uses or permitted by the competent authorities on a legal basis; or 5) claims giving doubt about the safety of similar food or which could arouse or exploit fear in the consumer. Misleading claims as incomplete comparatives and superlative and as to good hygienic practice should not be present on the product label[211], whereas the conditions of permitted claims are addressed[212] on principles of both relevant codex guidelines and national rules in each country. It has been indicated that a nutrition labelling should be provided in case a nutrition claim regarding the absence or non-addition of one or more nutrients is declared[213]. Apart from the principle guidelines, the CAC endorsed the Codex guidelines for use of nutrition and health claims (CAC/GL 23-1997) (FAO/WHO, 1997) in 1997 and latest revised in 2010, while the annex was adopted in 2009. From this document, a nutrition claim is defined as "any representation which states, suggests or implies that nutritional properties including but not limited to the energy value and to the content of protein, fat and carbohydrates, as well as the content of vitamins and minerals". It has been described that only nutrition claim relating to macronutrients and micronutrients for which Nutrient Reference Values (NRVs)[214] is laid down in the Codex Guidelines for Nutrition labelling. Besides, there are 3 types of nutrition claims classified by this guideline; 1) Nutrient content claim describing a level of the nutrient contained in a food; 2) Nutrient comparative claim referring a claim that compares the nutrient levels and/or energy value of two or more foods; and 3) Non-addition claim providing for any claim that an ingredient has not been either directly or indirectly added to a food. Comparing to the codex guidelines, EU provides more comparable definitions and types of nutrition claims rather than US and Thailand, except the non-addition claim is not specified in the EU regulations but it is included in the type of content claim, while only the permitted nutrition claims are able to use on supplement label[215]. Furthermore, the nutrition information for the supplements shall be provided in accordance with the article 8 of the directive 2002/46/EC[216]. FBOs must provide more specific nutrition information and nutrition and/or health claims as addressed under Article 30(1), and 30(2) of the requirement on nutrition labelling[217], respectively. In US, nutrient content claims (NNC) are defined similarly with the same type in the Codex guideline as well as a permitted list is also provided by the U.S. FDA based on scientific evidences. Even the definition of structure/function claims between codex and US are similar, classification of these claims is excluded from the health claims, unlike the codex guidelines because the structure/function claims describe the effect that a substance has on the structure or function of the body and do not make reference to the disease or health-related condition as

[211] Section 4 of the CAC/GL 1-1979, Rev. 1-1991
[212] Section 5 of the CAC/GL 1-1979, Rev. 1-1991
[213] Section 5.1 (vii) of the CAC/GL 1-1979, Rev. 1-1991
[214] Codex Guidelines on Nutrition Labelling (CAC/GL 2-1985), Section 2.6, p.2. Nutrient Reference Values (NRVs) are a set of numerical values that are based on scientific data for purpose of nutrition labelling and relevant claims. NRVs are based on levels of nutrients associated with nutrient requirements, or with the reduction in the risk of diet-related non-communicable diseases.
[215] Annex of the Regulation (EC) No. 1924/2006
[216] The third paragraph of Article 7 of the Regulation (EC) No. 1924/2006
[217] The first and second paragraphs of Article 7 of the Regulation (EC) No. 1924/2006 was replaced by the Article 49 of the Regulations (EU) No. 1169/2011

health claims but pre-authorisation by the U.S. FDA is not required (U. S. FDA, 2011c)[218]. Apart from warning statements, more specific requirements when presenting the claims are needed, especially in the disclaimer statement which is legally required for the structure/function claims. This disclaimer statement may support consumer to choose an appropriate supplements, however, it may not mean that the consumer protection can increase since one study on US consumers' perception on warning and disclaimer statement of dietary supplement (M. J. Mason et al., 2007) concluded that the mandate disclaimer is not working for safety and efficacy perception as intended by the U.S. FDA while the consumers do not consider the risk of the product even the disclaimer statement is performed. This study also revealed that a voluntary warning statement has a significantly important role to ensure that consumers have efficient information about both potential benefits and possible risks from consuming dietary supplements. Therefore, consumer perception and understanding on product information should be considered before regulating rules and be regularly evaluated to improve effective measures. Apart from EU and US, there are three types of nutrition claims in Thailand and are likely combined between EU and US systems, while definitions are mostly similar to Codex, EU, and US. Nutrient content claims and nutrient comparative claims are classified similarly to EU whereas the nutrient function claim is categorised as same as US. However, the condition and positive list for these claims are significantly based on Thai RDI and only allowed claims can apply for food supplements.

The codex guidelines[219] define a health claim as "any representation that state, suggests, or implies that a relationship exists between a food or a constituent of that food and health" and classify into three types; 1) Nutrient function claims referring to a nutrition claim that describes the physiological role of the nutrient in growth, development and normal functions of the body; 2) Other function claims concerning specific beneficial effects of the consumption of foods or their constituents based on total diet at normal functions or biological activities of the body; and 3) Reduction of disease risk claims relating to reduce risk of developing a disease or health-related condition after consumption of a food or its constituents in a context of the total diet. It has been clearly identified that the presentation of the reduction of disease risk claims should use appropriate language and reference to other risk factors to avoid consumers from misinterpretation. In addition, current relevant scientific substantiation[220] should be provided for evaluation, especially information on the physiological role of nutrients or on an accepted diet-health relationship and information on the composition of the product in relation to the physiological role, unless the relationship is based on a whole food or the research does not link to specific constituents of that food.

Comparing to the Codex guidelines, scientific evidences and pre-authorisation with a list of permitted health claims are addressed on the legal basis for health claims in EU, US, and Thailand as well as definition and purpose of the claims are mostly comparable. In contrast, main differences from the Codex standards are the classification of health claims and additional requirements on each type of the claims in EU and US. In EU, the reduction of disease risk claims and claims referring to children's development and health[221] are classified apart from other health claims[222] and full dossiers of evidence supporting the these claims are legally required to submit through an EC Health Claims authorisation process. In addition, the other health claims based on newly developed scientific data shall also be approved under the

[218] Section 21 U.S.C. 343(r)(6); 21 CFR 101.93.
[219] The CAC/GL 23-1997
[220] Annex of the CAC/GL 23-1997
[221] Article 14 of the Regulation (EC) No. 1924/2006
[222] Article 13 of the Regulation (EC) No. 1924/2006

authorisation process (Aisbitt, 2007). According to this process, responsible FBOs have to prepare a lot of scientific data and analytical works that may lead to obstacle in time-consuming and huge investment. Therefore, the authorisation process is based on proprietary data that means if the proprietary scientific data and relevant information have been used to apply for authorisation of a health claim, they cannot be used by another applicant until five years after the claims has been authorised in order to provide fair trade to the FBOs (Aisbitt, 2007).

In US, two types of health claims are allowed; authorised health claims and qualified health claims. Particular in the last category, the use of qualified health claims is permitted when the scientific evidence is not fully met with the "significant scientific agreement standard" of the U.S. FDA and they are authorised with using disclaimer statement to highlight the uncertain nature of the claims. This claim results in enhancing innovative food product development by a more flexible requirements which directly connect between diet and disease that is meaningfully different with Codex guidelines and EU rules. However, the qualified health claims has the potential to confuse consumers defining importance of these different statements (Aisbitt, 2007; Hasler, 2008). In Thailand, on the other hand, the legal requirements of health claim are on process of development based on the codex standards and three types of health claims following the Codex guidelines are proposed to set up.

In author's point of view, regulations on labelling and claims for food supplements in EU, US, and Thailand were developed based on the relevant codex standards leading to have similar definitions and purpose of using each claim, however, types of nutrition and health claims including additional requirements on the product labelling such as warning and disclaimer statements can differ from each other because of adequate and current scientific knowledge, national consumption data, political and economic issues including consumer perception that impact on risk management and decision making of legislative process.

For supplement advertisements, there is no internationally specific guideline for advertising food supplements, and the codex guidelines on nutrition and health claims are recommended to comprehensively apply both product label and advertisement[223]. Comparing to advertising requirements for food supplements in EU, US, and Thailand, main similarities are 1) definition of advertisements which cover all text, picture, print, broadcast, websites, catalogues, including directing market; and 2) a principle obligation for advertising food supplements that must be truthful, not misleading and scientifically substantiated. Additional requirements are also regulated in some countries, such as the pre-market approval of any food advertisement in Thailand, and a compulsory statement of advertising food supplements is required such as "this product should not be used as a substitute for a varied diet" and "this product is not intended to prevent, treat, or cure human disease" in EU and Thailand, respectively.

It has been indicated that development of the Codex guidelines are based on sound science and trade facilitation among WTO members while they are voluntary implementation, unless they are adopted into the national law leading to affect imported supplements (Porter, 2005). Similarities and differences of codex standards and national regulations on food supplements can be summarised as following table:

[223] Section 1 of the Codex guidelines for use of nutrition and health claims (CAC/GL 23-1997)

Table 17 Comparison between Codex standard on micronutrient food supplements and national regulations from EU, US, and Thailand (√: Similarities and X Differences)

Codex standard	EU	US	Thailand
1. Product			
1.1 Scope and Definition	√	√	√
1.2 Consideration of scientific data	√	√	√
1.3 Section of micronutrients	√ (Tool: a positive list)	X (divide by date of enforcement)	√ (Tool: a positive list)
1.4 Minimal and Maximum levels	√ (conceptually adopted from codex for both minimal and maximum levels)	X	√ (conceptually adopted from codex for the minimal level)
2. Premises	√ (HACCP base for all foods)	√ (CGMP for dietary supplements)	√ (GMP* for all foods)
3. Presentation			
3.1 Labelling	√	√	√
1) a term of "food supplement"	(food supplement)	(dietary supplement)	(dietary supplement)
2) Declaration of amount of micronutrient in numeric form per portion	√	√	√
3) Product information	√	√	√
4) Warning statements	√	√	√
5) Presence of nutrition labelling	√ (Nutrition fact)	√ (Supplement fact)	√ (Nutrition fact)
3.2 Claims			
1) Nutrition claims	√	√	√
- Definition			
- Types; 3 types	2 Types	2 Types	3 Types
(1) Nutrient content claim	(1) Nutrient content claims	(1) Nutrient content claims	(1) Nutrient content claims
(2) Nutrient comparative claim	(2) Nutrient comparative claim	Included in (1) type	(2) Nutrient comparative claims

Codex standard	EU	US	Thailand
		(2) Structure/Function Claims	(3) Nutrient function claims
(3) Non-addition claim	Included in (1) type	Included in (1) type	Included in (1) type
- Positive list of nutrition claims	√	√ (Only for (1) type)	√
- NRVs	Recommended Dietary Allowance (RDA)	Recommended Dietary Intake (RDI) or percentage of Daily value (%DV)	Thai Recommended Dietary Intake (RDI)
2) Health claims			
- Definition	√	√	√
- Type; 3 types	3 Types	2 Types	3 Types**
(1) Nutrient function claims	(1) Function claims	(1) Authorised health claims	(1) Nutrient function claims
(2) Other function claims	(2) Claims growth and development of children	(2) qualified health claims	(2) Other function claims
(3) Reduction of disease risk claims	(3) Disease risk reduction claims	-	(3) Reduction of disease risk claims
- Requirement on scientific substantiation	√	√	√
3.3 Advertisement			
- Follow codex guidelines on nutrition and health claims and no specific requirement	Directive on advertisements for all foods	Requirements for advertising dietary supplements	Requirements for advertising all foods

Remark: *GMP for dietary supplements is now on process of development.

** On the process of development

5.3 Aspect of pre-market control systems

The requirement of pre-market control depends on risk management and other factors impacting on food legislation. It has been shown the relation between food regulations and these relevant factors in US. The DSHEA Act of 1994 was primarily endorsed for industrial friendly so that the positive list of allowed micronutrients and the pre-market authorisation are not legally required for food supplements (S. A. Mason, 2010) to support the product innovation and avoid hinder entry to the market (Hanekamp & Bast, 2007). Unlike the US, both EU and Thailand regulations concern on safety and efficiency aspects of supplement and its presentation, the pre-market authorisation is placed on the regulatory system and required from FBOs to comply with these requirements before selling them to consumers. The pre-market authorisation plays an important mechanism to assess and evaluate a risk from the products, especially in new substances.

Moreover, all submitted documents for pre-market approval are a good source of scientific information for the competent authorities to further monitor the products and revise requirements. The GAO report (GAO, 2009) stated that lack of pre-market control of food supplements in US is a weakness of the regulatory system because of insufficiently scientific data and product detail leading to the U.S. FDA has incomprehensive knowledge about potential side effect of various products to monitor and take preventive actions. Moreover, this weakness affects consumers to have less information about the supplement so that they may not concern on potential side effects and may not consider the supplement as a factor if experiencing an adverse reaction. In case of a new substance, both EU and Thailand take into account on fully risk assessment and only the permitted ingredient can apply to the supplements, therefore, the period of time using for the risk assessment depends on completion of scientific document and current knowledge. In contrast, the new substance shall be notified within 75 days by the U.S. FDA prior to market so that the full risk-assessment may not completely apply while the purpose of this notification is not fully guarantee on safety aspect for consumers' health. In addition, the inadequate submitted data is still an obstacle for the competent agency. The U.S. FDA has deemed that even several hundred new dietary ingredient submissions received, less than 30% provided adequate safety data (Gershwin et al., 2010). In EU, an additional requirement for pre-market authorisation can differently enact in each MS but the purpose of implementation shall in line with the directive 2002/46/EC. An example of the Ireland case study, the notification procedure mandatorily require for food supplements being placed on the Irish market at the first time. Not only scientific documents regarding the supplement, but a model of product label shall be submitted through this system as well. Even this system is not used for fully risk assessment, it can support the work for monitoring and controlling the products after they are sold in the market in a case of incident or emergency problem. An Irish requirement that each individual sector shall follow the notification procedure may help competent officers to cross-check the reliable information of the same product by different stakeholders as well as to easily trace and track in case of non-compliance which is not required in the Thailand regulation. Therefore, it shows that the pre-market control system for food supplements in Ireland is more benefit.

Unlike product aspect, all premises shall be pre-registered by the competent authorities of EU, US and Thailand because the quality system based on either GMP or HACCP is a basis for food supplements brought to the market to primarily guarantee the quality and safety approach (Hanekamp & Bast, 2007; Pettman, 2011). However, it has diverged across three countries which mainly based on resources and capacities of competent agencies and FBOs as well as a huge challenge to harmonise the requirements of quality system for three regions.

For advertisements, the pre-market approval legally implement in Thailand so that all food advertisements including the supplements shall be approved by the Thai FDA. In EU, all advertisements shall comply with the EU directive 2006/114/EC, but any advertising food supplement particularly considers on requirements of product labelling and related claims. In US, there is no mandatory requirement for pre-permission of supplement advertisement, but the FBOs shall comply with the advertising requirements provided by the FTC. Cooperative works between the U.S. FDA and the FTC can reduce enormous work of the U.S. FDA but the harmonisation of enforcement policies and work procedures are not yet accomplished (Wollschlaeger, 2003; Yeung et al., 2006). Hence, the below table concludes comparison of pre-market control systems in EU, US, and Thailand.

Table 18 Comparison of pre-market control for food supplements from EU, US, and Thailand.

Requirement	EU (Ireland)	US	Thailand
Positive list of allowed micronutrients	√	-	√
Pre-market authorisation, in case of a new substance	√	-	√
Pre-notification in case of a new substance	-	√	-
Pre-market authorisation for premises	√	√	√
Pre-market authorisation for presentation - Labelling and claims - Advertisement	√ (Health Claims) -	√ (Health Claims) -	√ (Health Claims) √ (For all foods)
Major problems on pre-market control	- time-consuming for pre-market authorisation - maximum level is not yet approved by the EC	- insufficient resource of scientific data and product information - massive work for competent authorities - Public misperception on regulatory control	- time-consuming for pre-market authorisation - Maximum limits are based on Thai RDI that may result in exceeding consumption. - Regulations and positive list are less up-to-date.

5.4 Aspect of post-market control systems

According to EU, US, and Thailand regulations, the post-market control system is regularly implemented in order to ensure that the supplements sold on the market still comply with the regulations while the unsafe products can be rapidly detected and removed from the market. Many activities of post-market control are taken on both compulsory and voluntary basics but most of them are internal procedures available for competent agencies only resulting in limitation of accessible information on this study. The post-market measures mainly taken in the three countries are such as inspection and sampling procedure, monitoring and surveillance programmes, communication and information exchanging including training and education programmes for all stakeholders. A monitoring of public health in a relation to the intake of micronutrient food supplements is an effective tool for appropriate risk assessment and management, especially when the monitoring studies reveal potential risks associated with intake of the supplements (Hanekamp & Bast, 2007). Results of surveillance programme can also increase the public confidence since health-related problems associated with the use of supplements will be quickly identified and effectively addressed (Klein, 2004).

In EU, the post-market measure is not issued in the Directive 2002/46/EC but the actions may depend on managerial system of each MS. In case of Ireland, the specific sampling procedure and enforcement provision for food supplements are addressed under part 3 of the European Communities (Food Supplement) Regulation 2007 (S.I. No. 506 of 2007) and revised version (S.I. No. 355 of 2010). Similar to Thailand, the sampling procedure and criteria on non-compliance directly implement to all food supplements sold on the domestic market. In contrast, there are many sampling procedures in US depending on types of supplements and level of risk to consumers. Since the risk from food supplements is classified as a middle level, there are few samples taken from both domestic and imported supplements sold in US market due to limitation of human resource and budgets for analytical testing.

For monitoring and surveillance, the MANCP for 5-year implementation has been regularly developed by collaborating with relevant competent agencies in Ireland. It shows a successful plan to integrate work of relevant agencies with clear clarification of responsibility for each agency. According to this integrated national control plan, the human resources and budget for post-market control may be efficiently invested. Apart from the relevant official controls, a cooperative work with an independent body such as ASAI also supports the competent authorities in the view of consumer protection. Comparing to Ireland system, the monitoring and surveillance programme and mainly implemented by the U.S. FDA and Thai FDA and it is not officially integrated with an inspection plan at the state or provincial level in both US and Thailand; unless a voluntary collaboration is taken on case-by-case basis. It may assume that implementation of any measure or action may be less effective due to lack of systematically integrated control plan between central and provincial levels.

According to results of monitoring and surveillance programmes including consumer complaints from Ireland, US, and Thailand, the major problem on supplements is misleading information presenting on the label and advertisement as well as unproven claims of supplements. It is also recognised in EU, especially in imported products from third countries. When defective supplement is revealed, scientific information plays an essential role to support the competent authorities and FBOs for promptly investigating the cause of problem as well as providing appropriate measures for consumer protection. It has been issued that the U.S. FDA may fear with late response on faulty supplements due to inadequate scientific information. On the other hand, EU provides a more proactive measure based on a precautionary principle[224] in the case of uncertainty of scientific information while, in US and Thailand, clear scientific evidence shall be identified before further providing any measures. According to the rules from all three countries, punishment measures such as fine and/or imprisonment are provided for responsible stakeholders at all states of the supplement chain but the levels of measures may depend on impact of the non-compliance to consumers and public interest.

For the post-market control of food supplements, communication based on full-weight-of-evidence approach is also important but it could be considerably optimise the publics' knowledge of micronutrients concerning health and safety issues (Hanekamp & Bast, 2007). Communication network should be placed on the regulatory system and asked for all stakeholders to participate (Wollschlaeger, 2003). It has been shown that the network system has been successfully established and implemented in EU and Ireland. The RASFF is a legal communication tool[225] among EC, EFSA, and all MSs to notify any non-complied food

[224] Article 7 of the Regulation (EC) No. 178/2002
[225] Article 50 of the Regulation (EC) No. 178/2002

supplement both domestic production and imported from the third countries resulting in rapidly impeding the suspected product before entering to the territory. With clear responsibilities of each MS and EC and vivid procedure for communication and notification through the IT-base system, the RASFF provides scientific data and rapid communication leading to support achieving the post-market activity. In addition, the "Safety-Net" system has been actively implemented by relevant Irish authorities to monitor food supplements after they are notified by the FSAI. This system aims to exchange a list of permitted and prohibited supplements to all relevant inspectors in order to provide consistent and practical actions for monitoring and enforcing the laws. On the other hand, the adverse event reporting system is used in US and Thailand for monitoring food supplements which is only one-way communication mechanism leading to hardly communicate or get a feedback from the regulatory authority (Wollschlaeger, 2003). Moreover, a limited scope of compulsory reporting only a serious case causes the U.S. FDA to work difficultly. The lack of pre-market information also limits the U.S. FDA's capacity to investigate possible public health problem generated by the reporting system (Woo, 2007). Another study also addressed that the U.S. FDA has to rely heavily on the reporting of adverse events as a signal of possible public health concern. Between 1994 and 2000, the U.S. FDA took only 32 safety actions based on the adverse event reporting system, while an estimated 100 million American were taking dietary supplement (Gershwin et al., 2010). In Thailand, the adverse reporting system applies for all cases resulting from food supplements on the voluntary base, so very few cases regarding the supplement are reported with a low health effect. A communication channel for consumer complaints has been established in all three countries and rapid-response tools are regularly used for a more effective communication such as competent authority's website, hotlines, Facebook, and Twitter. It can serve as an effective two-way communication between competent authorities and consumers in order to increase their confidence and trust on the supplements as well as the received information is useful for further investigation and enforcement of non-compliant products.

To ensure that the relevant laws are fully enforced by all stakeholders, guidance on document submission, procedure of GMPs and risk assessment on food supplements to FBOs should be provided, whereas coordination with stakeholder and education of consumers are critical factors to improve better leverage existing resources as well as increase consumer understanding about the supplements (GAO, 2009). The study of empowerment for competent officers, FBOs, and consumer education in the chapter 4 presented that all EU, US and Thailand concerns on improvement of competent officers' skill as well as better understanding the regulations of FBOs resulting in many training programmes, guidance documents are published and available on the website of each competent authority. Particularly in consumers, education about the crucial importance of nutrition and the potential health benefits of a simple and affordable daily multi-vitamin and/or multi-mineral supplements is necessary in order to prevent exceeding consumption resulting in chronic disease as well as to achieve optimum health (Hanekamp & Bast, 2007). Nevertheless, no any accessible report or study on the evaluation after these training programmes and documents have been provided to assure that their knowledge is improved. Summary of post-market control systems in EU, US, and Thailand is presented in below table:

Table 19 Comparison of post-market control for food supplements from EU, US, and Thailand.

Requirement	EU (Ireland)	US	Thailand
Surveillance and monitoring plan	√ (MANCP)	√ (Single agency plan)	√ (Single agency plan)
Sampling	√ (For all kinds of supplements)	√ (depend on types and risk level of supplements)	√ (For all kinds of supplements)
Punishment	√	√	√
Communication network	√ (Two-way communication)	√ (One-way communication)	√ (One-way communication)
Training and education	√	√	√
Problem on post-market control	- Insufficient controlling unverified supplements sold on the internet and direct sale market from the third countries.	- Inadequate information about the supplements - Limitation of inspection resource - Less effective communication networking and information exchange -Insufficient controlling unverified supplements sold on the internet and direct sale market from the third countries.	- Limitation of inspection resource - Less effective communication networking and information exchange - Insufficient controlling unverified supplements sold on the internet and direct sale market from the third countries.

5.5 Summary

In a short conclusion, regulations on food supplements in EU, US, and Thailand are developed on the principle of relevant codex guidelines, risk analysis and scientific information that lead to have both similar and different measures covering 3Ps perspectives; Product, Premises, and Presentation. Similar to purposes of the Codex standards, major goals of all three countries are to protect consumer health, provide reliable information, and facilitate fair trade. In a comparison between the international guidelines and national regulations of EU, US, and Thailand, the scope of food supplement in the Codex document is more limited than the national regulations of these three countries, especially in botanical supplements which consistently increase in the world market share and international standard may be necessary for the trade facilitation and consumer health protection. The EC directive on food supplements is more comparable to the Codex guidelines while the requirements in US are more industrial friendly than the others. To protect consumer health when the requirements on product are less strict, the CGMPs rule on dietary supplements fully implement to all establishments in US. A pre-market control system is a proactive step to ensure that the supplement is safe before reaching consumers and would be a good scientific resource for further risk assessment and post-marketing control. However, the pre-market authorisation may affect innovation of new supplements and limitation on product availability for consumer choice so that the U.S. regulations do

not implement this system leading to have a biggest market share on the supplement in the world. A post-marketing control system is an important step applying in all three countries to monitor and verify that products sold on the market comply with national requirements as well as product information must not mislead to consumers. To have an effective post-market control, scientific information plays a crucial source for competent authorities to perform appropriate measures in a timely manner so that the U.S. FDA has obstacles on post-market control system. In addition, the consumer education is essential to have long-term prevention from unsafe or misleading supplements. Active network and information exchange are also essential activities for enhancing a functional monitoring plan and law enforcement in case of non-compliance.

Apart from specific regulations of food supplements, other measures of food safety system are also necessary to support the effectiveness of controlling system, especially in EU. The GFL addresses that all FBOs play responsibility to produce and distribute food complied as well as shall have close collaboration with the competent authorities in each step of the food chain, particularly in an incident, emergency, or crisis issue. The EFSA takes independent responsibility of risk assessment for food supplements to support risk manager as EC and MSs providing appropriate measures. In addition, traceability and RASFF network play important tools to rapidly and effectively communicate and investigate a problem on defective product. These supportive measures from both government and business parts could be recommended to strengthen the regulatory system of Thailand.

6. CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

From his comparative study, it has been clearly presented that the regulations of food supplements have been fully implemented in EU, US, and Thailand. All regulations are based on the Codex guidelines on vitamin and mineral supplements and considered on a risk analysis principle, domestic consumption, scientific evidence, and other factors such as economic and social aspects. Therefore, the national requirements are conformed to the codex guidelines as well as complied with the SPS and WTO agreements.

According to the organisation aspect in chapter 2, many organisations are involved in the regulatory systems for food supplements of EU, US, and Thailand in relation to the risk analysis principle. In each regulatory system, designed authorities are responsible for risk assessment and risk management bodies. In addition, the major targets of regulatory and control system of EU, US, and Thailand are purposely conducted to protect consumer health, control reliable information for consumer choice, and facilitate fair trade in both domestic and international markets. In comparison with three countries, the EU organisation is the most effective, especially in the establishment of EFSA because it is an independent agency, unlike US and Thailand systems, therefore this agency can fully support the scientific proven to the risk manager without any trade interference.

Along with the codex guideline and national regulations related to food supplements, definitions of supplement are obviously clarified in the chapter 3 that this product is classified as food, not drug and it can be distinguished from other similar products by the purpose of use, contained ingredients, and the product characteristics. Therefore, FBOs play a major role to determine category of the supplement, produce safe and bioavailable product, as well as provide reliable information to the consumers. However, comparing to codex guidelines, scope of food supplement under regulations and relevant amended provisions in EU, US, and Thailand are wider because they cover not only vitamins and minerals but also other substances such as amino acids, fatty acids, and botanical ingredients so that they mandate more safety and efficacy requirements for the product aspect.

Under the regulatory systems in EU, US, and Thailand described in chapter 3, the food supplements are safely controlled by 3Ps perspectives; 1. P-Product such as old and new substances, minimal and maximum safe level of micronutrient, other food safety requirements like food additives, contaminants, packaging, and pathogens; 2. P-Premises covers hygiene of firms, workers, and production including quality systems such as GMP or HACCP; and 3.P-Presentation includes labelling, nutrition and health claims, and advertisements. In EU, US, and Thailand, several activities applied to control food supplement before and/or after launching in the market also concern on the 3Ps perspectives in order to comply with relevant requirements.

The regulatory systems for food supplements in EU, US, and Thailand were described and analysed under chapter 3 and 5, respectively. In relation to the regulation on product perspective, The EC directive on food supplement is mostly conformed to recommendations under the codex guidelines, especially in the term and criteria on selection of micronutrients. In contrast, the US regulations are much flexible for selection of the substances and the level of each micronutrient in the supplements resulting in trade facilitation and product development. For Thailand, the requirements on the product aspect are similar to Codex and EU provisions, however, the setting of maximum level of micronutrient is not yet considered on other food

sources. Under the premises perspective, food hygiene and quality systems have been established in the regulatory system in all three countries because they primarily guarantee the quality and safety supplement product brought to the market. Unlike Codex guidelines, EU and Thailand regulations, the specific CGMPs rule for dietary supplement legally apply to US manufactures that helps to support the consumer protection when restriction of product obligation is soft. From the presentation perspective, several requirements on supplement labelling in EU, US, and Thailand follow the Codex guidelines, especially in use of "food supplement" or "dietary supplement", addressing a list of ingredients, amount, and warning statements. Besides, additional requirements on font sizes and background colours are mandated in US and Thailand regulations in order to clearly inform consumers. Nevertheless, the disclaimer statement in case of structure/function claims and qualified health claims is specifically required on US legal basis because there is no provision on pre-authorisation and safety evaluation for these claims before publication.

In view of the pre-market control system as analysed in chapter 5, EU and Thailand have similar mechanisms on pre-market authorisation for a new substance while a positive list and less strict requirements are provided for old substances that have already been evaluated on safety and efficacy basics. According to the pre-market authorisation, all scientific dossiers are evaluated and collected for further monitoring and investigating the products that sold on the market. Particular in Ireland, the notification procedure that legally requires individual sector to submit all information and label regarding the supplement being sold on the Irish market at the first time is an effective measure for all stakeholders because not only the FBOs at all stages of the supply chain should concern on scientific data supporting their product, but also the FSAI can cross-check information applied by different stakeholders, while all information is useful for relevant inspection bodies at the post-market control system. In contrast, the US regulations are much more flexible and friendly to the food industries since no provision on a positive list and pre-market authorisation of the new substances as well as the pre-approval of the health claims in US is also less strict, comparing to EU and Thailand. By these reasons, it would support US to have the biggest market share of supplement products in the world.

From the study on post-market controls in chapter 4, several activities are applied in EU, US, and Thailand, however based on comparative analysis in chapter 5, the system in Ireland as a case study shows high effectiveness, comparing to US and Thailand because of implementing the MANCP involved by all relevant authorities to monitor and control foods including food supplement sold on the Irish market, providing an active communication both intra- and inter- IT based systems with sufficient data sources on product and labelling information. Moreover, the traceability system required to be in place along supply chain under the GFL also supports the successful system on post-market control in EU. On the other hand, the post-market control system in US is less achievable for rapid consumer protection because of inadequate information of product and relevant scientific data resulting from no obligation on pre-market authorisation as well as a less effectiveness of communication and information exchange, especially in reporting mild and middle event cases from the FBOs which are still on voluntary basis. Similar to US, post-market control system in Thailand should be strengthened, particularly in updating scientific information regarding the supplements and improving a communication network. A major problem on post-market control commonly found in all three countries is unverified supplements sold on the internet and direct sale market that is a big obstacle for competent authorities to investigate and take proactive control actions, so the best solution for long-term prevention is to educate FBOs and consumers to have sufficient knowledge on legal compliance and selecting an appropriate supplement for themselves.

According to this comparative study, the EU regulatory system on food supplement is the most effective in the view of consumer protection due to full requirements on the regulations as well as several activities on pre- and post-market control systems. From these strict obligations, a major drawback is time-consuming and limitation of product development. Oppositely, the US system on food supplement is more industry friendly resulting from economic aspect that significantly taken into account by the risk management body. In Thailand, food supplements sold on the market are from both domestic production and importation. Even regulations and mechanisms have been implemented to control the safety and efficacy in supplements, there are still problems on non-compliance resulting in consumer health impact. Therefore, some mechanisms should be improved in order to protect consumer health and enhance trust from all stakeholders.

The added value of the comparative study is to understand that what and how the regulation of each country is implemented in order to control product safety as well as to protect consumer health. From the comparative study, strength and weakness of each system can be analysed, the similarities and differences of regulatory systems can be compared and therefore, some ideas for improving of the regulatory system in the interesting country can be proposed.

6.2 Recommendations

From this comparative study, strengthening regulatory system of food supplements focusing on vitamins and minerals in Thailand is necessary for a more effective consumer protection by following recommendations:

1. Improvement of scientific resources. It has been clearly presented in chapter 3 that the scientific information plays an important role on developing and revising the regulations. According to the regulations in Thailand described in chapter 3, the maximum level of vitamins and minerals in supplement is not yet considered on micronutrients from other food sources that may lead health effects, as well as the positive list of permitted micronutrients is less up-to-date. The scientific information is also an essential element for pre-market authorisation of new substances, product label and claims. In addition, this information can support the competent authority to provide proper activities of post-market control system. Therefore, scientific resources in relation to the food supplements should be improved.

2. Development of food hygiene and quality control system for food supplements. Since the quality system at the production step will significantly reduce risks from ingredients, packages, and distribution of the supplements, consumer confidence may increase if the products made from a manufacturer where the safety and quality system are put in place. In Thailand, the quality system for supplement production is based on GMP system as same as other food products described in chapter 3. Therefore, to have a better control system, a specific quality system for food supplement such as the CGMPs rule for dietary supplement in US should be developed.

3. Development of integrated control plan of post-market inspection. The monitoring plan of micronutrient supplements in Thailand is mainly implemented by the Thai FDA, while there is a voluntary collaboration with the provincial health offices on case-by-case basis. To have more sufficient control measures with resource limitation, the integrated plan at national level should be established. As the MANCP of Ireland explained in chapter 4, it is a useful tool that not only supports an effective post-market control, reduce workload and resource from the central agency, but also problems regarding supplement can be detected and investigated more quickly. The output from this plan would be also used as a scientific

source for further improvement on the regulations as well as the measures to be more efficient and comparative with the current situation.

4. Strengthening communication network. It has been described in chapter 4 and 5 that US and Thailand have less active communication network leading to late response on consumer protection, comparing to the EU system. IT-based networks that fully implemented in EU such as the Safety Net for communication among competent authorities of Ireland and the RASFF for rapid communication among the EC, the EFSA, and all MSs. present sufficient risk communication tools for timely consumer protection. Therefore, a fast communication and information exchange among stakeholders on legal basis should be applied in Thailand to assist better prevention measures in both regular situation and emergency case.

5. Enhancement of knowledge to all stakeholders. Problem on consumer confusion of food supplements with other similar products is still found in EU, US, and Thailand as discussed in chapter 3. For long-term prevention, the consumer education is necessary so that they can protect themselves by avoiding suspected product, and selecting an appropriate supplement for consumption. In addition, the FBOs play an important role to define product type, produce safe and efficacy supplement, and provide reliable information for consumer, therefore competent authorities should regularly encourage FBOs by providing guidelines, training programmes, and materials for legal compliance. Apart from FBOs and consumers, the relevant official controls also potentially involved in activities of post-market control system as described in chapter 4. Trainings on updated regulations and enforcement skills for these inspectors should be generally strengthened.

6. Improvement of general requirements on food safety to both government and business that may enhance an effectiveness of the regulatory system for food supplements. Like the EU system, the GFL requires establishment of the EFSA for improving risk assessment work, whereas mandates FBOs to place the traceability at all stages of the food chain as well as to be fully responsible on unsafe food products. These requirements significantly support the regulatory system of EU for higher level of consumer protection. Hence, these measures are suggested to legally implement in Thailand for all foods including food supplements.

7. More researches on other substances, particularly in botanical supplements. According market analysis of food supplements in chapter 2 and results on consumer survey in chapter 4, the botanical ingredients are extensively applied into food supplements and sold worldwide including Thailand. Because of natural ingredients, consumer have positive perception on the botanical products, however, the scientific evidences on safety and efficacy aspects are not readily available as stated in chapter 3. A problem on risks from botanical supplements occurs not only in Thailand but also in EU and USA. Therefore, proven results from the research in this area can effectively support risk assessment and risk management of this product.

REFERENCES

ACCSQ-TMHS. (2006). *Profile of Definition, Terminology, and Technical Requirement of Traditional Medicines and Health Supplements among ASEAN Member Countries*. Retrieved from http://www.aseansec.org/20258.pdf.

Aisbitt, B. (2007). Nutrition and Health Claims: the Facts on your Food: British Nutrition Fundation.

Analytics, K. (2012). Nutritional Supplements Market Report: 2012 Edition.

Aoude P., K. J., Wegener D. (2012). Chapter 3 Food supplementsGot Food? Recent Advance in Food Science and Technology: Massachusetts Academy of Math and Science. Retrieved from http://scientiareview.org/pdfs/257.pdf#page=31.

Arunanondchai J., P. C., Akaleephan C. (2007). *Tread and Health Diagnostic Tool: The Thailand Perspective*. Paper presented at the Paper prepared for the expert meeting on trade and health: A toolkit for national assessment, New Delhi, India. http://ihppthaigov.net/publication/attachresearch/231/chapter1.pdf

ASAI. (2010). ASAI Code: Health and Beauty Retrieved October 29, 2012, from http://www.asai.ie/entiresection.asp?Section_Num=8&Section_Desc=HealthandBeauty

ASAI. (2012). *The ASAI Annual Report 2011*. ASAI Retrieved from. http://www.asai.ie/documents/ASAI_ANNUAL%20REPORT%202011.pdf.

Bailey, R. L., Gahche, J. J., Lentino, C. V., Dwyer, J. T., Engel, J. S., Thomas, P. R., . . . Picciano, M. F. (2011). Dietary supplement use in the United States, 2003-2006. *Journal of Nutrition, 141*(2), 261-266. doi: 10.3945/jn.110.133025

Black, L. J., Ireland, J., Møller, A., Roe, M., Walton, J., Flynn, A., . . . Kiely, M. (2011). Development of an on-line Irish food composition database for nutrients. *Journal of Food Composition and Analysis, 24*(7), 1017-1023. doi: 10.1016/j.jfca.2011.01.015

BQSF.). Bureau of Quality and Safety of Food (BQSF): Roles and Responsibilities Retrieved September 2012, 2012, from http://www.dmsc.moph.go.th/webroot/BQSF/IndexMain.htm

Brookes, G. (2010). Economic Impact Assessment of the European Union (EU)'s Nutrition and Health Claims Regulation on the EU food supplement sector and market. GBC Ltd, UK.

Brownie, S. (2005). The development of the US and Australian dietary supplement regulations. What are the implications for product quality? *Complementary Therapies in Medicine, 13*(3), 191-198. doi: 10.1016/j.ctim.2005.06.005

Buttriss, J. L., & Benelam, B. (2010). Nutrition and health claims: The role of food composition data. *European Journal of Clinical Nutrition, 64*(SUPPL. 3), S8-S13. doi: 10.1038/ejcn.2010.203

CBI. (2012a). EU Legislation: Food supplements (vitamins and minerals) Retrieved September 27, 2012, from http://www.cbi.eu/marketinfo/cbi/docs/eu_legislation_food_supplements_vitamins_and_minerals

CBI. (2012b). Member States overview: Implementation of EU legislation on food supplements (vitamins and minerals) Retrieved September, 2012, from http://www.cbi.eu/marketinfo/cbi/docs/member_states_overview_implementation_of_eu_legislation_on_food_supplements_vitamins_and_minerals

Cheftel, J. C. (2005). Food and nutrition labelling in the European Union. *Food Chemistry, 93*(3), 531-550. doi: 10.1016/j.foodchem.2004.11.041

Chemist, G. Classification of Supplements as Food or Medicinal Products Retrieved from http://www.governmentchemist.org.uk/dm_documents/Classification%20of%20supplements%20as%20food%20or%20medicinal%20products_gZ1kQ.pdf

Codex. (2003). *Recommended international code of practice general principle of food hygiene (CAC/RCP 1-1996, Rev. 4-2003)*. FAO/WHO Retrieved from http://www.codexalimentarius.org/standards/list-of-standards/en/?provide=standards&orderField=fullReference&sort=asc&num1=CAC/RCP.

Codex. (2008). *Guidelines for the Validation of Food Safety Control Measures: CAC/GL 69-2008*. FAO/WHO Publication Retrieved from http://www.codexalimentarius.org/standards/list-of-standards/en/.

Codex. (2012a). List of active codex committee Retrieved September 11, 2012, from http://www.codexalimentarius.org/committees-task-forces/en/

Codex. (2012b). Lists of standards Retrieved September 12, 2012, from http://www.codexalimentarius.org/standards/list-of-standards/en/?provide=standards&orderField=fullReference&sort=asc&num1=CAC/GL

Coppens, P., Da Silva, M. F., & Pettman, S. (2006). European regulations on nutraceuticals, dietary supplements and functional foods: A framework based on safety. *Toxicology, 221*(1), 59-74. doi: 10.1016/j.tox.2005.12.022

Coppens, P., Delmulle, L., Gulati, O., Richardson, D., Ruthsatz, M., Sievers, H., & Sidani, S. (2006). Use of botanicals in food supplements: Regulatory scope, scientific risk assessment and claim substantiation. *Annals of Nutrition and Metabolism, 50*(6), 538-554. doi: 10.1159/000098146

Cox, A. (2010). Difference and Similarities in Food Supplement Regulations: Ireland Retrieved from http://www.lexmundi.com/Document.asp?DocID=2357

Crowley, R., & FitzGerald, L. H. (2006). The impact of cGMP compliance on consumer confidence in dietary supplement products. *Toxicology, 221*(1), 9-16. doi: 10.1016/j.tox.2006.01.011

DG_SANCO. (2010). *Country Profile: The organisation of food safety, animal health, animal welfare and plant health control systems-Ireland* European Commission Retrieved from http://ec.europa.eu/food/fvo/act_getProfile.cfm?pdf_id=39.

DG_SANCO. (2012). RASFF Portal: search page Retrieved October 31, 2012, from https://webgate.ec.europa.eu/rasff-window/portal/index.cfm?event=searchResultList

DMSc. (2011). Department of Medical Science (DMSc.): Introduction Retrieved September 20 2012, from http://www.dmsc.moph.go.th/dmsc/?page_id=6

DSHEA Summary & Analysis.). Retrieved September 17, 2012, from http://www.crnusa.org/leg.html#dshea

Dumoff, A. (2004). Legal Matter: Decoding the Codex Threat: Are limits on Access to Dietary Supplements Looming? *Alternative and Complementary Therapies, 10*(6), 343-349.

EAS. (2008). *Marketing Food Supplements, Fortified and Functional Foods in Europe: Legislation and Practice* (5 ed.).

Eberhardie, C. (2007). Nutritional supplements and the EU: is anyone happy? *Proceedings of the Nutrition Society, 66*, 508-511.

EC. (2006). *Discussion Paper on the setting of maximum and minimum amounts for vitamins and minerals in foodstuffs*. Retrieved from http://ec.europa.eu/food/food/labellingnutrition/supplements/discus_paper_amount_vitamins.pdf

EC. (2007a). *Answer to the letters addressed to Commissioner Kyprianou concerning the establishment of maximum amounts in food supplements*. Retrieved from http://ec.europa.eu/food/food/labellingnutrition/supplements/coll_answer_en.htm.

EC. (2007b). EUR-Lex: Case-law (Court of Justice) Retrieved September 24, 2012, from http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:62005J0319:EN:HTML

EC. (2012a). The Food and Veterinary Office – Role Retrieved September 17, 2012, from http://ec.europa.eu/food/fvo/what_en.htm

EC. (2012b). Food Contact Materials: Framework Regulation Retrieved October 2, 2012, from http://ec.europa.eu/food/food/chemicalsafety/foodcontact/framework_en.htm

EC. (2012c). Food Supplements Retrieved September 14, 2012, from http://ec.europa.eu/food/food/labellingnutrition/supplements/index_en.htm

EC. (2012d). *The Rapid Alert System for Food and Feed: 2011 Annual Report*. Office for Official Publication of the EC Retrieved from http://ec.europa.eu/food/food/rapidalert/docs/rasff_annual_report_2011_en.pdf.

EFSA. (2006). *Tolerable Upper Intake Levels for Vitamins and Minerals by the Scientific Panel on Dietetic products, nutrition and allergies (NDA) and Scientific Committee on Food (SCF)*. Retrieved from http://www.efsa.europa.eu/en/ndatopics/docs/ndatolerableuil.pdf

EFSA. (2009a). EFSA Press Release: assessment of vitamin and mineral sources used in food supplements Retrieved October 5, 2012, from http://www.efsa.europa.eu/en/press/news/ans090728.htm

EFSA. (2009b). Scientific opinion: Inability to assess the safety of vitamin B12-enriched yeast added for nutritional purposes as a source of vitamin B12 in food supplements and the bioavailability of vitamin B12 from this source, based *The EFSA Journal, 1126*, 1-6.

EFSA. (2011). Food Supplements: EFSA's roles and activities Retrieved September 13, 2012, from http://www.efsa.europa.eu/en/topics/topic/supplements.htm,

FAO/WHO. (1979). *Codex General Guidelines on Claims (CAC/GL 1-1979, Rev.1-1991)* FAO/WHO Retrieved from http://www.fao.org/docrep/005/Y2770E/y2770e05.htm.

FAO/WHO. (1997). *Guidelines for use of nutrition and health claims (CAC/GL 23-1997)*. FAO/WHO Retrieved from www.codexalimentarius.org/input/download/standards/351/CXG_023e.pdf

FAO/WHO. (2003). *Assuring Food Safety and Quality: Guidelines for Strengthening National Food Control Systems. FAO Food and Nutrition Paper no. 76.*: Joint FAO/WHO Publication Retrieved from http://www.fao.org/docrep/006/y8705e/y8705e00.htm#Contents.

FAO/WHO. (2006a). *Food safety risk analysis. A guide for national food safety authorities*. Rome: FAO and WHO Retrieved from ftp://ftp.fao.org/docrep/fao/009/a0822e/a0822e00.pdf

FAO/WHO. (2006b). *Understanding the Codex Alimentarius* (3 ed.): FAO/WHO.

FAO/WHO. (2011). *The Procedural Manual of the Codex Alimentarius Commission* (20 ed.).

FDA, T.). The Health Product Vigilance Centre (HPVC): Introduction of centre Retrieved November 2, 2012, from http://thaihpvc.fda.moph.go.th/thaihvc/Public/Webpage/main.jsp

Food Act B.E. 2522 (1979) (1979).

FDA, T. (1995). *Criteria and implementation guideline for Nutrification*

Notification of Ministry of Public Health No. 182 B.E. 2541 (1998), Re: Nutrition Labelling (1998).

Notification of Ministry of Public Health No. 193 B.E. 2543 (2000) Re: Production Processes, Production Equipments, and Foods Storages (2000).

Announcement of the Food and Drug Administration, Re: Certification of premises for imported foods (2001).

Notification of the Ministry of Public Health (No. 251) B.E. 2545 (2002) Re: Labelling of Food Obtained Through Certain Techniques of Genetic Modification / Genetic Engineering (2002).

FDA, T. (2004a). *FDA Thailand 2004*. Retrieved from http://www.fda.moph.go.th/eng/about/Figure1.pdf.

FDA, T. (2004b). Introduction: the Rural and Local Consumer Health Products Protection Promotion (RLCP) Division Retrieved September 19, 2012, from http://www.fda.moph.go.th/eng/rural/intro.stm

FDA, T. (2004c). Roles and Responsibilities Retrieved September 19, 2012, from http://www.fda.moph.go.th/eng/about/roles.stm

Notification of Ministry of Public Health: Food supplement (No. 293) (2005).

Announcement of the Thai Food and Drug Administration, Re: Evidences and documents in Application for Labelling of Food Supplements and Quality or Standards for Pathogenic Microorganisms (2006a).

Announcement of the Thai Food and Drug Administration, Re: Positive list of vitamins and minerals contained in dietary supplements (2006b).

FDA, T. (2007). *Guideline for registration and approval of dietary supplements: Revised version* Thai FDA publication Retrieved from http://newsser.fda.moph.go.th/food/pre/files/RabeabkarnFoodsupplement(2550).pdf.

Announcement of the Food and Drug Administration, Re: Criteria on advertising foods B.E. 2551 (2008) (2008a).

Announcement of the Food and Drug Administration, Re: Declaration of nutrient function claim (2008b).

FDA, T. (2010). *Excusive summary: development of monitoring and sampling plan for food quality and safety compliance*

FDA, T. (2011a). *The annual report of 2011* Thai FDA publication Retrieved from http://elib.fda.moph.go.th/library/Planweb/Doc/ANNUAL_REPORT2554.pdf.

FDA, T. (2011b). Bureau of Import and Export Inspection Retrieved September 19, 2012, from http://logistics.fda.moph.go.th:8080/fooddrug/view_page.php?id=5

FDA, T. (2011c). *Result of enforcement* Retrieved from http://www.fda.moph.go.th/www_fda/data_center/ifm_mod/nw/แจ้งผลการเปรียบเทียบปรับ_(กย._55).pdf.

FDA, T. (2012a). *Annual report of analytical results from health products* Thai FDA Publication Retrieved from http://elib.fda.moph.go.th/library/Planweb/admin/file_jobresult/News_รวมเล่มผลวิเคราะห์ปี54.pdf.

FDA, T. (2012b). Health Product Vigilance Centre (HPVC): News and Activities (The monthly report of September 2012) Retrieved November 2, 2012, from http://thaihpvc.fda.moph.go.th/thaihvc/Public/NewsAdr/uploads/hpvc_142.pdf

FDA, T. (2012c). Surveillance and Consumer Complaints service for health products: Annual reports 2011 Retrieved November 3, 2012, from http://newsser.fda.moph.go.th/hpsc/frontend/theme/info_operation.php?Submit=Clear

FDA, U. S.). Recalls, Market Withdrawals, & Safety Alerts Search: Dietary supplements Retrieved November 1, 2012, from http://google2.fda.gov/search?q=dietary+supplements&filter=0&proxystylesheet=FDAgov-recalls&output=xml_no_dtd&sort=date%253AD%253AL%253Ad1&site=FDAgov-recalls&getfields=*&requiredfields=recall_category&client=FDAgov-recalls&ie=UTF-8&ip=137.224.233.85&access=p&entqr=3&entqrm=0&oe=UTF-8&ud=1&start=0

Dietary Supplement Health and Education Act of 1994 (1994).

Code of Federal Regulations Title 21, Part 10 – Administrative practices and procedure (Subpart B: general administrative procedure) (2000).
Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301 et seq. Amended through December 31,2004 (2004).
FDA, U. S. (2005). *Guidance for Industry: A Dietary Supplement Labelling Guide*. Retrieved from http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/DietarySupplements/DietarySupplementlabelingguide/default.htm.
Dietary Supplement and Nonprescription Drug Consumer Protection Act of 2006. (2006a).
FDA, U. S. (2006b). Testimony: The Regulation of Dietary Supplements: A Review of Consumer Safeguards Retrieved November 2, 2012, from http://www.fda.gov/NewsEvents/Testimony/ucm112576.htm
Current Good Manufacturing Practice in Manufacturing, Packaging,

Labeling, or Holding Operations for Dietary Supplements (2007).
FDA, U. S. (2010). Testimony: Oversight of Dietary Supplements Retrieved November 2, 2012, from http://www.fda.gov/NewsEvents/Testimony/ucm213531.htm
FDA, U. S. (2011a). Food Compliance Programmes: Dietary Supplements-Import and Domestic (Implementation Date: 03/26/2010) includes Pen & Ink Changes as of 07/08/10 to Parts I and II Retrieved November 2, 2012, from http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/ComplianceEnforcement/ucm071547.htm
FDA, U. S. (2011b). Food Contact Substances (FCS) Retrieved October 12, 2012, from http://www.fda.gov/Food/FoodIngredientsPackaging/FoodContactSubstancesFCS/default.htm
FDA, U. S. (2011c). Guidance for Industry: A Food Labelling Guide (8. Claims) Retrieved November 29, 2012, from http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/ucm064908.htm
Code of Federal Regulations Title 21 (Part 4)- Nutritional Quality Guidelines for Foods: Subpart B – Fortification Policy (2012a).
FDA, U. S. (2012b). Dietary Supplements Retrieved October 12, 2012, from http://www.fda.gov/food/dietarysupplements/default.htm
FDA, U. S. (2012c). Dietary Supplements- Adverse Event Reporting Retrieved November 1, 2012, from http://www.fda.gov/Food/DietarySupplements/Alerts/ucm111110.htm#users
FDA, U. S. (2012d). Food Safety Modernization Act: Registration Retrieved October 12, 2012, from http://www.fda.gov/Food/FoodSafety/FSMA/ucm314178.htm
FDA, U. S. (2012e). Genetically Engineered Plants for Food and Feed Retrieved September 26, 2012, from http://www.fda.gov/Food/Biotechnology/default.htm
FDA, U. S. (2012f). Responses to Questions about Codex and Dietary Supplements Retrieved September 12, 2012, from http://www.fda.gov/food/dietarysupplements/GuidanceComplianceRegulatoryInformation/ucm113860.htm
FDA., T. Food supplement and Thai social value. Retrieved from http://elib.fda.moph.go.th/library/default.asp?page2=subdetail&id_L1=27&id_L2=18725&id_L3=1011
FDA., T. (2011). *Arresting direct sale of dietary supplements*. Retrieved from http://www.fda.moph.go.th/www_fda/data_center/ifm_mod/nw/ข่าวจับบ.ขายตรงผ.เสริมอาหาร__ส่ง_27 สค_55_.pdf.
Federal Ministry of Food, A. a. C. P.). CCNFSDU website Retrieved September 11, 2012, from https://www.ccnfsdu.de/index.php?id=309
Flynn, A., Moreiras, O., Stehle, P., Fletcher, R. J., Müller, D. J. G., & Rolland, V. (2003). Vitamins and minerals: A model for safe addition to foods. *European Journal of Nutrition, 42*(2), 118-130. doi: 10.1007/s00394-003-0391-9
European Communities (Food Supplement) Regulation 2007, S.I. No. 506 of 2007 C.F.R. (2007).
FSAI. (2009a). Article 13(5) Health Claims Retrieved November 30, 2012, from http://www.fsai.ie/science_and_health/nutrition_and_health_claims/article_13(5).html
FSAI. (2009b). National Food Surveillance Retrieved October 29, 2012, from http://www.fsai.ie/legislation/food_legislation/official_control_of_foodstuffs/national_food_surveillance.html
FSAI. (2009c). *A research study into consumers' attitude to food labelling*. FSAI publication Retrieved from http://www.fsai.ie/enforcement_audit/monitoring/food_monitoring_surveillance/labelling.html.
FSAI. (2010a). The Annual Report 2010 Retrieved October 29, 2012, from http://www.fsai.ie/resources_publications.html
European Communities (Food Supplement) (Amendment) Regulation 2010 (S.I. No. 355 of 2010) C.F.R. (2010b).

FSAI. (2010c). FAQs: Food Supplements Retrieved October 29, 2012, from http://www.fsai.ie/faq/food_supplements.html
FSAI. (2010d). *Guidance Note No.21: Food Supplements Regulations and Notifications (Revision 1)*. Retrieved from http://www.fsai.ie/resources_publications.html.
FSAI. (2010e). *Information on Nutrition and Health Claims and Food Supplements*. Retrieved from http://www.lenus.ie/hse/bitstream/10147/104959/1/Nutrition.pdf.
FSAI. (2011). The Annual Report 2011 Retrieved October 29, 2012, from http://www.lenus.ie/hse/handle/10147/235211?mode=full
FSAI. (2012a). *Aide Memoire for Food Supplement Establishment Inspections*. FSAI Retrieved from http://www.fsai.ie/science_and_health/food_supplements.html.
FSAI. (2012b). Article 14 Health Claims Retrieved November 30, 2012, from http://www.fsai.ie/science_and_health/nutrition_and_health_claims/article_14.html
FSAI. (2012c). *Checklist for Food Supplement Establishment Inspections*. FSAI publication Retrieved from http://www.fsai.ie/resources_publications.html.
FSAI. (2012d). Enforcement Retrieved November 28, 2012, from http://www.fsai.ie/enforcement_audit/enforcement.html
FSAI. (2012e). Irradiated Food Surveillance Retrieved October 29, 2012, from http://www.fsai.ie/enforcement_audit/monitoring/surveillance/irradiated_food.html
FSAI. (2012f). Labelling Monitoring and Surveillance Retrieved October 29, 2012, from http://www.fsai.ie/enforcement_audit/monitoring/food_monitoring_surveillance/labelling.html
FSAI. (2012g). Nutrition and Health Claims Retrieved November 30, 2012 from http://www.fsai.ie/content.aspx?id=194&terms=health+claims
FSAI&DAFF. (2007). *The National Control Plan for Ireland for the period from 1st January 2007 to 31st December 2011*. Retrieved from http://www.agriculture.gov.ie/media/migration/farmingschemesandpayments/nationalcontrolplanforfoodfeedandwelfare/NationalControlPlan20072011.pdf.
FTC. (2001). *Dietary Supplements: An Advertising Guide for the Industry*. Retrieved from http://business.ftc.gov/documents/bus09-dietary-supplements-advertising-guide-industry
FTC. (2003). Dietary supplements advertising cases 1984-July 15, 2003 Retrieved November 2, 2012, from http://www.ftc.gov/bcp/reports/dietadvertisingcases.shtm
FTC. (2007). Law Enforcement Retrieved November 2, 2012, from http://www.ftc.gov/bcp/menus/resources/enforcement.shtm
FTC. (2012). About the Bureau of Consumer Protection Retrieved September 17, 2012, from http://www.ftc.gov/bcp/about.shtm
GAO. (2009). *Dietary Supplements: FDA Should Take Further Actions to Improve Oversight and Consumer Understanding. Report to Congressional Requesters*. GAO Public Affair Retrieved from http://www.gao.gov/assets/290/285372.pdf.
Gershwin, M. E., Borchers, A. T., Keen, C. L., Hendler, S., Hagie, F., & Greenwood, M. R. C. (2010). Public safety and dietary supplementation. In M. E. Gershwin & M. R. C. Greenwood (Eds.), *Annals of the New York Academy of Sciences* (Vol. 1190, pp. 104-117).
Gibson, J. E., & Taylor, D. A. (2005). Can claims, misleading information, and manufacturing issues regarding dietary supplements be improved in the United States? . *Journal of Pharmacology and Experimental Therapeutics, 314*(3), 939-944. doi: 10.1124/jpet.105.085712
Gilsenan, M. B. (2011). Nutrition and health claims in the European Union: A regulatory overview. *Trends in Food Science and Technology, 22*(10), 536-542. doi: 10.1016/j.tifs.2011.03.004
Rules and Regulations: Current Good Manufacturing Practice in Manufacturing, Packaging, Labelling, or Holding Operations for Dietary Supplements; Final Rule, Federal Register, 72(121): 34752-34958 C.F.R. (2007).
Public Law 11-353-111th Congress (2011).
Greene, H. L., Prior, T., & Frier, H. I. (2001). Foods, health claims, and the law: comparisons of the United States and Europe. *Obesity research, 9 Suppl 4*, 276S-283S.
Greger, J. L. (2001). Dietary supplement use: Consumer characteristics and interests. *Journal of Nutrition, 131*(4 SUPPL.), 1339S-1343S.

Hanekamp, J. C., & Bast, A. (2007). Food supplements and European regulation within a precautionary context: A critique and implications for nutritional, toxicological and regulatory consistency. *Critical Reviews in Food Science and Nutrition, 47*(3), 267-285. doi: 10.1080/10408390600737748

Hasler, C. M. (2008). Health claims in the United States: An aid to the public or a source of confusion? *Journal of Nutrition, 138*(6), 1216S-1220S.

Hatchcock, J. (2001). Dietary supplements: how they are used and regulated. *Journal of Nutrition, 131*(3s), 1114S-1117S.

Hathcock, J. (2005). Myths and Facts on Codex and WTO. Retrieved from Council for Responsible Nutrition website: http://www.crnusa.org/pdfs/CodexMythsFacts022505.pdf

Havel, R. J. (1999). Dietary supplement or drug? The case of Cholestin. *The American Journal of Clinical Nutrition, 69*, 175-176.

Health, M. o. P. (2008). Missions of Ministry of Public Health Retrieved September 19, 2012, from http://www.moph.go.th/moph2/index4.php?page=include_page2&id=45

HHS, U. S.). About HHS Retrieved September 17, 2012, from http://www.hhs.gov/about/

HHS, U. S.). The Office of Intergovernmental and External Affairs: Regional Office Retrieved September 17, 2012, from http://www.hhs.gov/iea/regional/index.html

HSE. (2012). *Annual Report and Financial Statements 2011*. HSE publication Retrieved from http://www.hse.ie/eng/services/Publications/corporate/annualreport2011.html.

Intarapanich P., H. S. (2012). The meeting report of GMP for Traditional Medicine & Health Supplement. 1-18. Retrieved from http://iodinethailand.fda.moph.go.th/food_54/data/news/2555/september/doc1859/D1859-23.pdf

Isichaikul, T. (2002). Development of control system for dietary supplements in Thailand

Jiang, T., & Zhang, S. (2009). Stringent laws and regulations for dietary supplements. *Drug Information Journal, 43*(1), 75-81.

Kampopong, N. (2004). Advertising food by direct sale system (pp. 1-63).

Kearney, J. (2010). Food consumption trends and drivers. *Philosophical Transactions of the Royal Society B: Biological Sciences, 365*(1554), 2793-2807. doi: 10.1098/rstb.2010.0149

Khaopolsri, W. (2004). Analysis of situations and pattern of advertising dietary supplements in variety TV programme and resolutions

Klein, C. J. (2004). LSRO Report: Adverse Event Monitoring Programs for Dietary Supplements: Life Science Research Office (LSRO).

Krutmann, J., Humbert, P., Karajiannis, H., & Fish, C. (2011). Legal Aspects: How Do Food Supplements Differ from Drugs, Medical Devices, and Cosmetic Products? *Nutrition for Healthy Skin* (pp. 167-180): Springer Berlin Heidelberg.

Law, N. Y. S. T. F. o. L. t. (2005). *Dietary Supplements: Balancing Consumer Choice and Safety* Retrieved from http://www.health.ny.gov/regulations/task_force/docs/dietary_supplement_safety.pdf.

Lichtenstein A.H. , R. R. M. (2005). Essential Nutrients: Food or Supplements? Where Should the Emphasis Be? *The Journal of the American Medical Association, 294*(3), 351-358.

Lin, J. R., Lin, Y. S., Kao, M. D., Yang, Y. H., & Pan, W. H. (2011). Use of supplements by Taiwanese adults aged 19-44 during 2005-2008. *Asia Pacific Journal of Clinical Nutrition, 20*(2), 319-326.

Marcus, D. M., & Grollman, A. P. (2012). The consequences of ineffective regulation of dietary supplements. *Archives of Internal Medicine, 172*(13), 1035-1036. doi: 10.1001/archinternmed.2012.2687

Mason, M. J., Scammon, D. L., & Fang, X. (2007). The impact of warnings, disclaimers, and product experience on consumers' perceptions of dietary supplements. *Journal of Consumer Affairs, 41*(1), 74-99. doi: 10.1111/j.1745-6606.2006.00069.x

Mason, S. A. (2010). Dietary Supplement Regulation: A Comparative Study. *Journal of Transnational Law and Policy, 20*, 103-127.

Meulen B.M.J. van der, V. M. v. d. (2008). *European Food Law Handbook* (1 ed.). The Netherlands: Wageningen Academic Publishers.

Miller, D. M. (2008). Legal matters: Impact of international product regulations on consumer access to, and the manufacturing of, dietary supplements: The need for health freedom advocacy. *Alternative and Complementary Therapies, 14*(1), 43-47. doi: 10.1089/act.2008.14102

Milner, J. A. (2000). Functional foods: The US perspective. *American Journal of Clinical Nutrition, 71*(6 SUPPL.), 1654S-1659S.

Mulholland, C. A., & Benford, D. J. (2007). What is known about the safety of multivitamin-multimineral supplements for the generally healthy population? Theoretical basis for harm. *American Journal of Clinical Nutrition, 85*(1), 318S-322S.

NCBE. (2006). Genetically-modified food: US regulations Retrieved September 26, 2012, from http://www.ncbe.reading.ac.uk/ncbe/gmfood/usregulations.html

ODS.). Mission, Origin, and Mandate Retrieved september 17, 2012, from http://ods.od.nih.gov/About/MissionOriginMandate.aspx

Petroczi, A., Taylor, G., & Naughton, D. P. (2011). Mission impossible? Regulatory and enforcement issues to ensure safety of dietary supplements. *Food and Chemical Toxicology, 49*(2), 393-402.

Pettman, S. (2011). Perspectives on Regulation on Food Supplements. *Sight and Life, 25*(3), 62-63.

Porter, D. V. (2005). Dietary Supplements: International Standards and Trade Agreements (D. S. P. Division, Trans.) *CRS Report for Congress* (pp. 1-6): Congressional Reserch Service.

Reinert, A., Rohrmann, S., Becker, N., & Linseisen, J. (2007). Lifestyle and diet in people using dietary supplements: A German cohort study. *European Journal of Nutrition, 46*(3), 165-173. doi: 10.1007/s00394-007-0650-2

Reportlinker. (2010). Vitamin and Supplement Industry: Market Research Reports, Statistics and Analysis.

Reuterswärd, A. L. (2007). The new EC Regulation on nutrition and health claims on foods. *Scandinavian Journal of Food and Nutrition, 51*(3), 100-106. doi: 10.1080/17482970701685625

Schwitters, B., Achanta, G., van der Vlies, D., Morisset, H., Bast, A., & Hanekamp, J. C. (2007). The European regulation of food supplements and food fortification: Intended normal use - The ultimate tool in organising level playing field markets and regulations, or how to break the fairy ring around 'other substances'. *Environmental Law and Management, 19*(1), 19-29.

Silano, V., Coppens, P., Larrañaga-Guetaria, A., Minghetti, P., & Roth-Ehrang, R. (2011). Regulations applicable to plant food supplements and related products in the European Union. *Food and Function, 2*(12), 710-719. doi: 10.1039/c1fo10105f

Siró, I., Kápolna, E., Kápolna, B., & Lugasi, A. (2008). Functional food. Product development, marketing and consumer acceptance-A review. *Appetite, 51*(3), 456-467. doi: 10.1016/j.appet.2008.05.060

Taylor, C. L. (2004). Regulatory Frameworks for Functional Foods and Dietary Supplements. *Nutrition Reviews, 62*(2), *55-59*. doi: 10.1301/nr.2004.feb.*55-59*

Teerawat, O. (2002). Nutrition labelling of dietary supplements Retrieved from http://elib.fda.moph.go.th/library/fulltext1/private/picture.asp?temp=12673

Tetens, I., Biltoft-Jensen, A., Spagner, C., Christensen, T., Gille, M. B., Bügel, S., & Rasmussen, L. B. (2011). Intake of micronutrients among Danish adult users and non-users of dietary supplements. *Food and Nutrition Research, 55*. doi: 10.3402/fnr.v*55*i0.7153

Texas, D. o. S. H. S. o. (2011). Dietary Supplement: Food Group. Retrieved September 18, 2012, from http://www.dshs.state.tx.us/foods/dietary.shtm

Tiasuwan, N. (1999). Analysis and study on control measure for dietary supplement (pp. 1-35).

Timbo, B. B., Ross, M. P., McCarthy, P. V., & Lin, C. T. J. (2006). Dietary Supplements in a National Survey: Prevalence of Use and Reports of Adverse Events. *Journal of the American Dietetic Association, 106*(12), 1966-1974. doi: 10.1016/j.jada.2006.09.002

Tippayakunanon, N. (1996). Import control system for dietary supplements (pp. 1-96). Retrieved from http://elib.fda.moph.go.th/library/fulltext1/private/picture.asp?temp=3512

Verhagen, H., Vos, E., Francl, S., Heinonen, M., & van Loveren, H. (2010). Status of nutrition and health claims in Europe. *Archives of Biochemistry and Biophysics, 501*(1), 6-15. doi: 10.1016/j.abb.2010.04.012

Wollschlaeger, B. (2003). The Dietary Supplement and Health Education Act and Supplements: Dietary and Nutritional Supplements Need No More Regulations. *International Journal of Toxicology, 22*(5), 387-390.

Woo, J. J. Y. (2007). Adverse event monitoring and multivitamin-multimineral dietary supplements. *American Journal of Clinical Nutrition, 85*(1), 323S-324S.

WTO. (2012). Sanitary and Phytosanitary Measures: Text of the Agreement Retrieved September 12, 2012, from http://www.wto.org/english/tratop_e/sps_e/spsagr_e.htm

Yeung, M. T., Hobbs, J. E., & Kerr, W. A. (2006). Accessing US and EU markets for nutraceuticals and functional foods: Legislative and technical barriers facing agribusiness marketers. *Journal of International Food and Agribusiness Marketing, 19*(1), 53-79. doi: 10.1300/J047v19n01_04

Zlotkin, S., Siekmann, J., Lartey, A., & Yang, Z. (2010). The role of the Codex Alimentarius process in support of new products to enhance the nutritional health of infants and young children. *Food and Nutrition Bulletin, 31*(2 SUPPL.), S128-S133.

ANNEX I

LIST OF TECHNICAL DOSSIER PREPARED FOR SUBMISSIONS FOR SAFETY EVALUATION OF SOURCE OF NUTRIENTS OR OF OTHER INGREDIENTS PROPOSED FOR USE IN THE MANUFACTURE OF FOODS.

1. Administrative data

1.1 Purpose of the request, including statement on the category/categories of food in which the source is intended to be used. (E.g. Commission Directive 2002/46/EC Food supplements – Annex I and/or Annex II)

1.2 Name of the petitioner, address, telephone, telefax, e-mail.

1.3 Name of the manufacturer(s) of the source (if different from above), address, telephone, telefax, e-mail.

1.4 Name of the person responsible for the dossier, telephone, telefax, e-mail.

1.5 Date of submission of the dossier.

1.6 Table of contents of the dossier.

2. Technical data

2.1 Identity of source

2.1.1 Chemical name (if any) according to IUPAC nomenclature rules.

2.1.2 CAS number (if any).

2.1.3 Synonyms, trade names, abbreviations.

2.1.4 If a mixture: constituents of the mixture and proportion of each component.

2.1.5 Molecular and structural formulae.

2.1.6 Molecular weight.

2.1.7 Spectroscopic data which allow the identification of the source, e.g.IR, UV, NMR, MS, etc.

2.1.8 Purity in percentage; method of determination; data printout (chromatograms, spectra, etc).

2.1.9 Impurities: nature, percentage and methods of determination.

2.1.10 Description of physical state.

2.2 Specifications

2.2.1 The proposed chemical and microbiological specifications of the source should be submitted in a format modelled on recent EU or other internationally accepted specifications.

2.2.2 If no detailed specifications are available, a statement that the source proposed for use conforms to existing purity criteria laid down EU legislation, or, in their absence, conforms to generally acceptable purity criteria given by other national or international bodies.

2.3 Manufacturing process

2.3.1 Origin and method of manufacture of the source, production controls and quality assurance.

2.3.2 For chemically synthesised sources, factors such as reaction sequence, side reactions, purification and preparation of the product to be commercialised which may assist in determining likely impurities and their influence on the toxicological evaluation.

2.3.3 For sources extracted from naturally occurring substances, information on extraction procedure(s).

2.4 Methods of analysis in food

2.4.1 Analytical methods for the determination of the source and (where relevant) its degradation products in foods.

2.4.2 Analytical methods should be given in full, except where the analytical methods used are well established, in which case they may be given by reference only.

2.5 Reaction and fate in food(s) to which the source is added

2.5.1 The stability and any degradation products or reaction products appearing as a result of processing, storage and preparation of foods containing the source.

2.5.2 Any possible effect of instability on biological properties including nutrient value.

2.6 Case of need and proposed uses

2.6.1 Justification for this particular source (not just a general justification for the nutrient or other ingredient).

2.6.2 Types of products in which it is intended to use the source, and Mode of incorporation.

2.6.3 Quantities to be added to these products.

2.7 Exposure

2.7.1 Known or anticipated human exposure to the source from food and other routes of exposure, including amount (e.g. maximum and average intake or exposure), frequency and other factors influencing exposure. Information should also be given on any other sources of human exposure to the same substance (e.g. from drinking water, consumer products, etc.)

2.7.2 The above exposure calculations should be explained, including any assumptions made. Where possible, information on consumption of the foods where the source is used or intended to be used, including variations affecting particular sections of the population (e.g. by age, sex, disease, etc.).

2.8 Information on existing authorisations and evaluations

2.8.1 Information on any existing national authorisations and evaluations and/or evaluations by other bodies on the source should be provided.

3. Biological and toxicological data

3.1 Bioavailability of the nutrient or other ingredient from its source following oral consumption; from human data, from in vitro or animal studies, or from information on analogous substances.

3.2 Subsequent metabolic fate of the source and biological distribution.

3.3 Any known interactions of the source with other components in the diet.

3.4 Impact of the source on the intestinal milieu and on the absorption of other nutrients.

3.5 Toxicological data on the source.

3.5.1. The available data should be submitted in the first instance. The extent of the data needed will depend on safety considerations in relation to the fate of the source in the body. Any deviations from requirements already established for food additives (SCF, 2001b) should be justified.

4. Sources that consist of, contain, or are derived from genetically modified organisms

4.1 In the case of sources of nutrients or of other ingredients that contain or are derived from genetically modified organisms, information should also be provided on the genetically modified organism(s) in accordance with the guidance given by the Scientific Committee on Food.1

5. Annexes

5.1 Complete bibliographical list of references.

5.2 Copies of all references listed.

ANNEX II

SUMMARY OF RISK ASSESSMENT PROCESS IN DEVELOPMENT OF ULS FOR MICRONUTRIENTS

Step	Activities
1. Hazard identification	All adverse health effects resulted from each nutrient are outlined by scientifically clinical data or experiments, particularly from human studies. In case of insufficient data on human studies, other experimental data both in vivo and in vitro may also be used. Six key issues that can be concerned on the data evaluation of experimental studies are; 1) *Evidence of adverse effects on humans*. Based on these studies, results representing in "adverse effect" is cautiously considered to comply with definition of the adverse effect and correct decision. 2) *Causality*. The causal significance of an exposure-effect association between nutrient intake and adverse effect is importantly indicated by epidemiological studies including demonstration of a temporal relationship, consistency, strength of association, and a dose-response relationship. 3) *Relevance of experimental data*. All relevant studies should be taken into consideration from different animals, routes of exposures, duration of exposures and relevance of exposures by human populations. 4) *Mechanisms of adverse effects*. Knowledge at molecular or cellular level related to adverse effect process is able to assist in data interpretation. 5) *Quality and completeness of the data base*. High quality and comprehensiveness of data base influences data interpretation and ULs establishment 6) *Identification of distinct and highly sensitive sub-populations*. In case by case, the derivation of the UL may be included.
2. Hazard characterization	It is important to consider does response assessment which addresses the relationship between does of nutrient and adverse effect based on both qualitative and quantitative evaluations. It also involves other key components such as 1) *Data selection*. It results in data evaluation process 2) *Identification of NOAEL (or LOAEL) and critical endpoint*. These values are identified and the most sensitive endpoint is selected to protect against all other adverse effects. 3) *Uncertainty assessment*. Uncertainty factors considered from different observed data, inter- and intra-spices from the animal studies could be significantly concerned for derivation of ULs 4) Derivation of an UL. The UL is derived by dividing the NOAEL (or LOAEL) by the uncertainty factor. ULs are derived for different life-stage groups using relevant data.
3. Exposure assessment	Distribution of usual daily nutrient intakes in the general population group has to be evaluated.
4. Risk characterization	Risk of nutrient intake is described based on the scientific uncertainties associated with the UL estimation. An estimate of intake for population groups may also include, if the data are available. In case of insufficient data to estimate a UL, the highest level of intake where is reasonable confident in data on the absence of adverse effects should be indicated.