A preliminary assessment of approval rates of health claims in the EU: Regulation 1924/2006

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Abstract

The time of satisfying hunger has passed. People are now eager to improve their quality of life. Besides taking enough nutrition from food, consumers have started to focus on the importance of food as a way to maintain or improve their health. Studies show that nutrients from food can maintain and even improve the health of consumers (Kwak and Jukes, 2001). In 1994 food with enhanced health benefit, here referred as functional foods, have been introduced in Europe and became popular shortly after. With the emergence of the functional food market, the potential risk of asymmetric information between manufacturers and consumers became evident and the concern about the truthfulness of the health claims appeared. In order to regulate the market and guarantee the truthfulness of the health claims European council and parliament in 2006 emanated Regulation 1924/2006, setting the criteria for products' health claims to be approved.

Article 13.1, Article 13.5 and Article 14 of this regulation define the types of health claims and regulate their approval. Article 13.1 includes general claims and it is based on previous knowledge between a food/food constituent and health. Article 13.5 focuses on newly developed products. Article 14 concentrates on disease risks reduction or children's health (Mariotti et. al., 2010). Health claims have high rejection rates: 1) 92 per cent of Article 13.1 claims have been rejected, 2) 80 per cent of Article 13.5 claims have been rejected and 3) 65 per cent of Article 14 claims have been rejected (Greer and Kurzer, 2013). This thesis provides a background introduction for my Master thesis, giving graphical representations of the approval rates of Article 13.1 claims, and Article 13.5 and Article 14 claims combined.

In order to analyze the factors that may influence the approval rates of Article 13.1, Article 13.5 and 14 claims, a literature review is conducted from the official website of European Food Safety Authority (EFSA). 984 submitted claims have been collected for Article 13.1 claims; while 188 submitted claims have been collected for Article 13.5 and Article 14 claims. We assess the approval and rejection rates conditionally on the different features of the protocols submitted using pie charts. For Article 13.1 the five major groups of features of the submitted protocols are: food categories group, food ingredients group, function of claims, submitted studies and re-submitted protocols. For Article 13.5 and Article 14 claims we identified seven groups of features of the submitted protocols: type of claim, food categories group, food ingredients group, function of claims, submitted studies, countries (countries/cities manufactures come from) and

re-submitted protocols.

According to the results, if a protocol is submitted for an Article 13.1 claim for food ingredients with mineral and vitamin, phytosterol, there are circa 50 per cent claims approved, while none of the protocols have been approved for probiotics products. Dental and brain health claims, have circa 30 per cent of claims approved (dental with 32 per cent, 30 per cent for brain). However, only 7 per cent of claims have been approved for intestinal health. If a protocol includes in situ studies and RCT clinical trials, it will have a higher chance to be approved: protocols with in situ studies have 90 per cent approval rate while those with RCT clinical have 72 per cent. However, only 4 per cent claims have favorable outcomes submitted a protocol with single arm studies.

If a manufacturer submits protocols for Article 13.5 and Article 14 claims, the submissions related to vitamin, phytosterols and carbohydrates-electrolyte solution have circa 67 per cent approval rate. When submitted protocols carry the health function of bone and joint, vision and dental, the percentage of approval is circa 50 per cent. 39 per cent claims are approved when protocols include studies of meta-analysis. Moreover, if the manufactures come from Germany, Belgium or France, the rate of approval is circa 45 per cent. However, manufactures submitting protocols for probiotics, those who did not mention references for studies supporting their claims studies, or who have used single arm studies, had all their claims rejected. Studies relate to weight and muscle, only have 6 per cent of claims being approved.

Only 38 per cent of Article 13.1 claims and 23 per cent of Article 13.5 and Article 14 claims for re-submitted protocols have been approved. The approval probabilities of re-submitted protocols in health claims are still low. If manufactures obtain a negative outcome (to be rejected by NDA panel) for the first submission, they will have a large chance to be failed on re-submitting protocols as well. Since the process of re-submitting protocols provided by the EFSA may not assist manufactures to increase the approval rate, the EFSA faces a transparency issue.

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1. Introduction

1.1 Background

In the last decades, food demand has changed considerably. Food is not only used to satisfy hunger anymore. Some studies proved that food can both provide nutrients to humans and prevent problems of aging and diseases (Kwak and Jukes, 2001). Functional food is a natural or processed food, which benefits to maintain body functions instead of treating diseases directly. As shown by the expansion of functional food products in Europe, consumers increasingly consume functional food as a means to prevent diseases and to reduce discomfort (Heasman, 2001). In order to establish a Europe-wide functional food science, in 1995 the International Life Sciences Institute (ILSI) was founded to provide evidence of whether specific nutrients can affect positively a human body function (Sanders, 1998).

With the expansion of unclear labels of functional food, consumers do not trust the European functional food market (Bech-Larsen and Scholderer, 2007). In 2006 the EU nutrition and health claim regulation 1924/2006 was launched by the Council and Parliament to protect consumers from being misled and to reduce information asymmetry (Verhagen et al, 2010; Bech-Larsen and Scholderer, 2007). This regulation divided the claims allowed on food products in two types, health claims and nutrition claims. Health claims are about the relationship between a food or its ingredients and human health. Nutrition claims state whether the food or its constituents has beneficial nutritional properties (Bech-Larsen and Scholderer, 2007). The regulation classifies health claims according to Article 13.1, Article 13.5 and Article 14. Claims under Article 13.1 are "general function" claims which are related to growth and development. Claims falling under Article 13.5 are based on new and/or proprietary data. Article 14 claims focuses on disease risks reduction or children's health (Mariotti et al, 2010; Valls, 2013).

The assessment of the EFSA has resulted in circa 92 per cent of claims of Article 13.1 claims, 80 per cent of Article 13.5 claims and 65 per cent of Article 14 claims being rejected (Greer and Kurzer, 2013). In this research we will present graphical results of the approval rates of Article 13.1 claims and a combination of Article 13.5 and Article 14 claims.

1.2 Thesis structure

This report consists of five chapters. Chapter 1 provides background of this thesis. In chapter 2 the literature review about the development of the regulation and the definition of the health claims is conducted. Chapter 3 describes the methodology of this thesis. Chapter 3 will also introduce the approved claims submitted for different health claims. Chapter 4 illustrates the approval claims' probability conditionally to the evidences provided to EFSA for Article 13.1, Article 13.5 and Article 14. Chapter 5 contains the conclusions.

2. Literature review

2.1Functional foods in Europe

In mid 1990s, functional food products were firstly introduced into the German market and then into other European countries thanks to some international food manufactures, e.g. Nestle, Danone, Unilever, Kellogg, and Quaker Oats (Menrad, 2000). The concept of functional foods was first defined by UK ministry of Agriculture, Fisheries and food (MAFF) in 1995. The initial definition of a functional food was "a food that can provide medical or physiological benefit, other than purely nutritional effect" (Richardson, 1996). International Life Science Institute (ILSI) Europe stated that "a functional food is satisfactorily demonstrated to affect beneficially one or more target functions in body, beyond adequate nutritional effects, in the way that is relevant to either an improved state of health and well-being and/or reduction of risk of disease" (Diplock et al, 1999). Moreover functional foods in EU could only be consumed in a "normal food pattern", thus it was not allowed to produce products such as pills, tablets and capsules (Ohama et al, 2006). The EU launched the regulation of 1924/2006 nutrition and health claims to regulate the use of health claims in the EU functional foods market. This regulation protect consumers from being misled and reduces information asymmetry (the product itself does not have the function which is stated on labels or in advertisements) (Asp and Bryngelsson, 2008; Niva, 2007).

2.2 Regulation 1924/2006 on nutrition and health claims

In 2006, the Regulation 1924/2006 on nutrition and health claims was launched

(Verhagen et al, 2010). This regulation regulates the use of the claims in two types, nutrition claims and health claims. Health claims are about the function of food (for example how certain food or ingredients influence the physical or mental of human body). Nutrition claims state nutritional properties of food/constituent (such as vitamin and fiber) (European Community, 2006). The purpose of this regulation is to ensure the truthfulness of health claims and to protect consumers from being misled (Bech-Larsen and Scholderer, 2007). This regulation sets the criteria for products' health claims to be approved and classifies health claims in two different categories: disease risk reduction or to children's development or health claims (Article14) and others claims (Article 13). Claims which fall under article 13 are further divided in two groups. Article 13.1 claims comprise "general function" claims relating to growth, development, and functions of the body. They should be based on generally accepted evidence and could be used by any manufacturers as long as the conditions of use are kept. Article 13.5 claims pertain to general function claims based on new and/or proprietary data. This type of claim is particularly relevant for manufacturers who have invested in innovation and wish to protect their claim and/or underpinning scientific data. Based on the regulation and scientific evidences provided by manufactures, the European Food Safety Authority (EFSA) give scientific opinions on whether claims are to be approved or not (European Community, 2006).

2.3 The European Food Safety Authority (EFSA)

With the appearance of food and feed problems, the general public was not satisfied with the EU food safety system. In 2002 the European Food safety Authority (EFSA) was founded, aiming to renovate the trust of the public in the EU food safety system (Silano and Silano, 2008). This authority focuses on food and feed safety issues, which also include animal welfare and health. The missions of EFSA are (Silano and Silano, 2008):

- To provide scientific advice or support in food and feed safety;
- To evaluate emerging or potential risks;
- To collect and process data for monitoring risks in food and feed area;
- To build communication and network between institutions and manufactures about the potential risks in food and feed sectors in Member States.

The EFSA gives their scientific advises on the food or feed issues to manufactures and consumers. The EFSA has five different panels. The panel of Nutrition and Allergies (NDA) deals with problems related to nutrition. Thus NDA panel processes Claims under regulation of 1924/2006.

Once manufacturers' submitted applications are approved by NDA panel, the products can be sold in the market with health claims. Otherwise health claims cannot appear on the labels of products and in the advertisements (Mariotti et al, 2010).

2.4 Health claims

According to the information from the European Food Safety Authority (EFSA), circa 44,000 health claims have been submitted by member states between 2008 and 2010. All those health claims have been consolidated into a list of 4,637 claims，to be evaluated by the NDA panel. In 2011 the NDA panel published 341 scientific opinions of Article 13.1, which were drawn from 4,637 claims (Lusk, Roosen and Shogren, 2011). For Article 13.5 and Article 14, over 280 health and nutrition claims were submitted by member states (Verhagen et al, 2010). In 2010 the NDA panel published 88 scientific opinions on Article 13.5 and Article 14 claims (Brookes, 2010).

The application of Article 13.1 is different from Article 13.5 and Article 14. Article 13.1 is based on previous knowledge between food/its constituents and health, meanwhile, the authorization of Article 13.1 does not need to be individually applied (Brookes, 2010). Article 13.5 is more focus on the relationship between new products/its constituents (not well known) and the function (O'Connor, 2011). Article 14 focuses on "disease reduction", health and development of children. It states that the food or its constituent helps to reduce the risks of human diseases (Mariotti et al, 2010).

3. Material and Method

3.1 Data collection

The information regarding the features of Article 13.1, and Article 13.5 and 14 protocols submitted to EFSA, as well as the outcome of the review by the NDA panel (rejection or approval) has been collected from the EFSA Journals. Different information has been selected as the relevant factors on influencing the approval probabilities of Article 13.1, and Article 13.5 and Article 14 claims. 984 submitted claims are collected from scientific opinions of Article 13.1 claims. Furthermore, 188 submitted claims are collected from scientific opinions of Article 13.5 and Article 14 claims as well. From the Article 13.1 submitted claims I identified 42 factors divided into 6 major groups: outcome of the

application, food categories, food ingredients, function of the claims, submitted evidence/studies and whether a protocol was submitted before (i.e. a re-submitted protocol). 67 features of the protocols submitted for Article 13.5 and Article 14 were identified, which belong to one of 8 major groups: outcome of the submission, type of claims, food categories, food ingredients, function of claims, submitted evidence/studies (definition in Table 3-1), countries that manufactures come from and whether a protocol was re-submitted. More detailed information can be found elsewhere in my Master thesis.

3.2 Definition of the studies that manufactures' submitted

According to the Regulation 1924/2006, the health claims should be based on science, thus the manufactures should submit studies to prove their products/constituents scientifically qualified to have a health claim. In the data collected there are 11 main types of studies (not included specific definition on published and unpublished studies) which have been submitted by the manufactures: human intervention studies, human observation studies, in vivo studies, in vitro studies, ex vivo studies, in situ studies, random control trials, random clinical trials, meta-analyses, single arm studies and reviews. Table 3-1 shows the definition of studies that manufactures submitted to EFSA.

Table 3-1 Definition of submitted studies published by EFSA

Studies	Definitions
Human intervention studies [1]	Carry out intervention studies on human volunteers to find the evidence of nutrients from products (Pool-Zobel et al, 1997).
Human observation studies	Find the relationship between nutrients of food and human health by using quantitative analysis (Vlaanderen et al, 2008).
In vivo studies	To build experiment in whole living organism (Perkel, 2007).
In vitro studies [1]	In a laboratory environment build an experiment in test tube (Tice et al, 2000)
Ex vivo studies	Ex vivo conducts the experiment outside the living environment.
In situ studies	In situ is a study which is the intermediate between in vivo and in vitro (Hamperl, 1959).
Random Control Trials	RCT is studies that randomly allocated to have on or other

	alternative treatment under study (Chalmers et al, 1981).
Random Clinical Trials	Participants were randomly allocated in different treatment group, the participants can also choose the group they want to go. After treatment, the outcome of different treatments will be compared (Little et al, 2012).
Single arm studies	A study that with uncontrolled group (Paulus, 2013).
Meta-analysis	Combing the outcome of the topic from different studies (Rothman et al, 2008).
Reviews	Could be the book reviews, conference reviews and etc (Korn and Korn, 2000).

Note: [1] include both published and unpublished studies.

Source: EFSA website, October, 2009- Jan, 2014

3.3 Approved health claims

3.3.1 Article 13.1 claims

Table 3-2 shows that 246 submitted claims have been approved by the NDA panel. According to this table, it is clear that a large percentage ofvitamin[1] and mineral[2] claims have been approved. The approval rate of each claim will be illustrated in chapter 3.4.

Table 3-2: Approved Article 13.1 claims

Nutrition	Function
Alpha cyclodextrin	reduction of post prandial glycaemic responses
Dried plums of 'prune' cultivars (Prunusdomestica L.)	maintenance of normal bowel function
Creatine	Increaseinphysical performance during short-term, high intensity, repeated exercise bouts.
Monacolin K from red yeast rice	maintenance of normal blood LDL cholesterol concentrations
Chitosan	maintenance of normal blood LDL-cholesterol concentrations

Vitamin D[1]	normal absorption of calcium
Protein	growth or maintenance of muscle mass
Calcium[2]	maintenance of normal bone
Alpha-linolenic acid (ALA)	maintenance of normal blood cholesterol concentrations
Replacement of mixtures of saturated fatty acids (SFAs) as present in foods or diets with mixtures of polyunsaturated fatty acids (PUFAs)	maintenance of normal blood LDL-cholesterol concentrations
Lactase	breaking down lactose
Pectins	maintenance of normal blood cholesterol concentrations
Chromium	maintenance of normal blood glucose concentrations
Choline	maintenance of normal liver function
Oat	barley grain fiber and increase in faecal bulk
Melatonin	reduction of sleep onset latency
L-tyrosine	Contribution to normal synthesis of catecholamines
Beta-glucans from oats and barley	reduction of post-prandial glycaemic responses
Linoleic acid	maintenance of normal blood LDL-cholesterol concentrations
Foods with reduced lactose content	Decreasing gastro-intestinal discomfort caused by lactose intake in lactose intolerant individuals
Very low calorie diets (VLCDs)	reduction in body weight
Carbohydrate-electrolyte solutions	Enhancement of water absorption during exercise
Carbohydrate-electrolyte solutions	maintenance of endurance performance
Sodium[2]	maintenance of normal muscle function
Foods with reduced amounts of sodium	maintenance of normal blood pressure
Arabinoxylan produced from wheat endosperm	Reduction of post-prandial glycaemic responses
Glycaemic carbohydrates	maintenance of normal brain function
Fructose	Reduction of post-prandial glycaemic responses

Rye fiber	changes in bowel function
Fats	normal absorption of fat-soluble vitamins
Intense sweeteners	reduction of post-prandial glycaemic responses
Intense sweeteners	Maintenance of tooth mineralization by decreasing tooth demineralization
Sugar-free chewing gum with fluoride	maintenance of tooth mineralization
Replacement of mixtures of saturated fatty acids (SFAs) as present in foods or diets with mixtures of monoun saturated fatty acids (MUFAs) and/or mixtures of polyunsaturated fatty acids (PUFAs),	maintenance of normal blood LDL cholesterol concentrations
Caffeine	increase in endurance performance
Sugar replacers xylitol, sorbitol, mannitol, maltitol, lactitol, isomalt, erythritol, D-tagatose, isomaltulose, sucralose and polydextrose	maintenance of tooth mineralization by decreasing tooth demineralization
Sugar replacers xylitol, sorbitol, mannitol, maltitol, lactitol,isomalt, erythritol, D-tagatose, isomaltulose, sucralose and polydextrose	reduction of post-prandial glycaemic responses
Walnuts	improvement of endothelium-dependent vasodilation
Carotene	maintenance of the normal function of the immune system
Resistant starch	reduction of post-prandial glycaemic responses
Caffeine	increased alertness and increased attention
Choline	contribution to normal lipid metabolism
Choline	maintenance of normal liver function
Choline	contribution to normal homocysteine metabolism
Water	maintenance of normal physical and cognitive functions
Polyphenols in olive	protection of LDL particles from oxidative damage
Activated charcoal	Reduction of excessive intestinal gas accumulation(ID 1938) and reduction of

	bloating
L arginine	maintenance of normal ammonia
Sugar-free chewing gum with carbamide	plaque acid neutralisation
Copper[2]	maintenance of the normal function of the nervous system
Copper[2]	maintenance of the normal function of the immune system
Copper[2]	contribution to normal energy-yielding metabolism
Betaine	contribution to normal homocysteine metabolism
Docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA)	maintenance of normal brain function
Docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA)	maintenance of normal vision
Meat or fish	improvement of non haem iron absorption
Oleic acid intended to replace saturated fatty acids (SFAs) in foods or diets	maintenance of normal blood LDL-cholesterol concentrations
Foods with reduced amounts of saturated fatty acids (SFAs)	maintenance of normal blood LDL cholesterol concentrations
Lactulose	reduction in intestinal transit time
Plant sterols and plant stanols	maintenance of normal blood cholesterol concentrations
Vitamin A (including β-carotene) [1]	maintenance of normal vision
Vitamin A (including β-carotene)[1]	maintenance of normal skin and mucous membranes
Iron [2]	formation of red blood cells and haemoglobin
Iron[2]	oxygen transport
Iron[2]	contribution to normal energy-yielding metabolism
Iron[2]	reduction of tiredness and fatigue
Hydroxypropyl methylcellulose (HPMC)	reduction of post-prandial glycaemic responses
Folate	Contribution to normal psychological functions
Folate	cell division
Folate	contribution to normal amino acid synthesis

Manganese[2]	Contribution to normal formation of connective tissue
Manganese[2]	contribution to normal energy yielding
Protein	maintenance of normal bone
Protein	growth or maintenance of muscle mass
Selenium[2]	maintenance of normal hair
Selenium[2]	maintenance of normal nails
Selenium[2]	maintenance of normal thyroid function
Selenium[2]	protection of DNA, proteins and lipids from oxidative damage
Selenium[2]	maintenance of the normal function of the immune system
Iodine[2]	contribution to normal cognitive and neurological function
Iodine[2]	contribution to normal energy-yielding metabolism
Iodine[2]	contribution to normal thyroid function and production of thyroid hormones
Vitamin B6[1]	contribution to normal cysteine synthesis，contribution to normal homocysteine metabolism
Vitamin B6[1]	contribution to normal energy-yielding metabolism ; contribution to normal psychological function；reduction of tiredness and fatigue
Docosahexaenoic acid (DHA)	Maintenance of normal (fasting) blood concentrations of triglycerides
Docosahexaenoic acid (DHA)	maintenance of normal brain function
Docosahexaenoic acid (DHA)	maintenance of normal vision
Chromium	Contribution to normal macronutrient metabolism
Chromium	Maintenance of normal blood glucose concentrations
Biotin	maintenance of normal skin and mucous membranes
Biotin	maintenance of normal hair
Biotin	Contribution to normal psychological

	functions
Biotin	Contribution to normal macronutrient metabolism
Vitamin E[1]	protection of DNA, proteins and lipids from oxidative damage
Chloride as Na-, K-, Ca-, or Mg-salt[2]	Contribution to normal digestion by production of hydrochloric acid in the stomach
Konjacmannan	reduction of body weight
Fluoride	maintenance of tooth mineralisation
Vitamin C[1]	reduction of tiredness and fatigue
Vitamin C[1]	Contribution to normal psychological functions
Vitamin C[1]	regeneration of the reduced form of vitamin E
Vitamin C[1]	contribution to normal energy-yielding metabolism
Vitamin C[1]	maintenance of the normal function of the immune system
Vitamin C[1]	protection of DNA, proteins and lipids from oxidative damage
Vitamin B12[1]	contribution to normal neurological and psychological functions
Vitamin B12[1]	Contribution to normal homocysteine metabolism
Vitamin B12[1]	reduction of tiredness and fatigue
Vitamin B12[1]	cell division
Calcium[2]	maintenance of normal bone and teeth
Calcium[2]	regulation of normal cell division and differentiation
Live yoghurt cultures	improved lactose digestion
Molybdenum	contribution to normal amino acid metabolism
Niacin	reduction of tiredness and fatigue
Niacin	contribution to normal energy-yielding metabolism
Niacin	contribution to normal psychological functions

Niacin	maintenance of normal skin and mucous membranes
Magnesium[2]	contribution to normal psychological functions
Magnesium[2]	maintenance of normal muscle contraction
Riboflavin (vitamin B2)[1]	Contribution to normal energy-yielding metabolism
Riboflavin (vitamin B2)[1]	maintenance of normal skin and mucous membranes
Riboflavin (vitamin B2)[1]	maintenance of normal vision
Riboflavin (vitamin B2)[1]	maintenance of normal red blood cells
Riboflavin (vitamin B2)[1]	reduction of tiredness and fatigue
Riboflavin (vitamin B2)[1]	protection of DNA, proteins and lipids from oxidative damage
Riboflavin (vitamin B2)[1]	maintenance of the normal function of the nervous system
Eicosapentaenoic acid (EPA), docosahexaenoicacid (DHA), docosapentaenoic acid (DPA)	maintenance of normal blood pressure
Eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), docosapentaenoic acid (DPA)	improved absorption of EPA and DHA
Pantothenic acid	mental performance
Pantothenic acid	reduction of tiredness and fatigue
Pectins	Reduction of post-prandial glycaemic responses
Pectins	Maintenance of normal blood cholesterol concentrations
Zinc[2]	maintenance of normal skin
Zinc[2]	DNA synthesis and cell division
Zinc[2]	contribution to normal protein synthesis
Zinc[2]	maintenance of normal serum testosterone concentrations
Zinc[2]	Contribution to normal carbohydrate metabolism
Zinc[2]	maintenance of normal hair
Zinc[2]	maintenance of normal nails
Thiamin	Contribution to normal psychological

	functions
Wheat bran fiber	increase in faecal bulk, reduction in intestinal transit time
Potassium	Maintenance of normal muscular and neurological function
Potassium	maintenance of normal blood pressure
Melatonin	alleviation of subjective feelings of jet lag
Guar gum	Maintenance of normal blood cholesterol concentrations
Vitamin D[1]	normal function of the immune system and inflammatory response
Vitamin D[1]	maintenance of normal muscle function
Lodine[2]	thyroid function and production of thyroid hormones
Lodine[2]	energy-yielding metabolism
Lodine[2]	maintenance of skin
Beta glucans	maintenance of normal blood cholesterol concentrations
Iron[2]	formation of red blood cells and haemoglobin
Iron[2]	oxygen transport
Iron[2]	energy-yielding metabolism
Iron[2]	function of the immune system
Iron[2]	cognitive function
Iron[2]	cell division
Sugar free chewing gum	plaque acid neutralisation
Sugar free chewing gum	maintenance of tooth mineralisation
Sugar free chewing gum	reduction of oral dryness
Lactase enzyme	breaking down lactose
Niacin	energy-yielding metabolism
Niacin	function of the nervous system
Niacin	Maintenance of the skin and mucous membranes
Calcium[2]	maintenance of bones and teeth
Calcium[2]	muscle function and neurotransmission
Calcium[2]	blood coagulation
Calcium[2]	energy-yielding metabolism

Calcium[2]	function of digestive enzymes
Copper[2]	protection of DNA, proteins and lipids from oxidative damage
Copper[2]	function of the immune system
Copper[2]	maintenance of connective tissues
Copper[2]	energy-yielding metabolism
Copper[2]	function of the nervous system
Copper[2]	maintenance of skin and hair pigmentation
Copper[2]	iron transport
Manganese[2]	protection of DNA, proteins and lipids from oxidative damage
Manganese[2]	maintenance of bone
Manganese[2]	energy-yielding metabolism
Vitamin C[1]	protection of DNA, proteins and lipids from oxidative damage
Vitamin C[1]	collagen formation
Vitamin C[1]	function of the nervous system
Vitamin C[1]	function of the immune system, function of the immune system during and after extreme physical exercise
Vitamin C[1]	non-haem iron absorption
Vitamin C[1]	energy-yielding metabolism
Phosphorus	function of cell membranes
Phosphorus	energy-yielding metabolism
Phosphorus	maintenance of bone and teeth
Biotin	energy-yielding metabolism
Biotin	macronutrient metabolism
Biotin	maintenance of skin and mucous membranes
Biotin	maintenance of hair
Biotin	function of the nervous system
Calcium and vitamin D[1]	maintenance of bone
Fluoride	maintenance of tooth mineralisation
Vitamin A[1]	function of the immune system
Vitamin A[1]	function of the immune system
Vitamin A[1]	maintenance of skin and mucous membranes
Vitamin A[1]	maintenance of vision

Vitamin A[1]	metabolism of iron
Pantothenic acid	energy-yielding metabolism
Pantothenic acid	mental performance
Pantothenic acid	synthesis and metabolism of steroid hormones, vitamin D and some neurotransmitters
Folate	blood formation
Folate	homocysteine metabolism
Folate	function of the immune system
Folate	cell division
Folate	maternal tissue growth during pregnancy
Glucomannan	maintenance of normal blood cholesterol concentrations
Alpha linolenic acid	maintenance of normal blood cholesterol concentrations
Vitamin B12[1]	red blood cell formation
Vitamin B12[1]	cell division
Vitamin B12[1]	energy-yielding metabolism
Vitamin B12[1]	function of the immune system
Vitamin B6[1]	protein and glycogen metabolism
Vitamin B6[1]	function of the nervous system
Vitamin B6[1]	red blood cell formation
Vitamin B6[1]	function of the immune system
Vitamin B6[1]	regulation of hormonal activity
Zinc[2]	function of the immune system
Zinc[2]	protection of DNA, proteins and lipids from oxidative damage
Zinc[2]	maintenance of bone
Zinc[2]	cognitive function
Zinc[2]	fertility and reproduction
Zinc[2]	metabolism of fatty acids
Zinc[2]	maintenance of vision
Magnesium[2]	electrolyte balance
Magnesium[2]	energy-yielding metabolism
Magnesium[2]	neurotransmission and muscle contraction including heart muscle

Magnesium[2]	cell division
Magnesium[2]	maintenance of bone
Magnesium[2]	maintenance of teeth
Magnesium[2]	protein synthesis
Selenium[2]	protection of DNA, proteins and lipids from oxidative damage
Selenium[2]	function of the immune system
Selenium[2]	thyroid function
Thiamine	energy-yielding metabolism
Thiamine	cardiac function
Thiamine	function of the nervous system
Vitamin K[1]	maintenance of bone
Vitamin K[1]	blood coagulation
Vitamin D[1]	maintenance of bone and teeth
Vitamin D[1]	absorption and utilisation of calcium and phosphorus and maintenance of normal blood calcium concentrations
Vitamin D[1]	cell division
EPA, DHA, DPA	maintenance of normal blood pressure
EPA, DHA, DPA	maintenance of normal (fasting) blood concentrations of triglycerides
Meal replacements	weight control and reduction in body weight

Note: [1]= Vitamin products, [2]=mineral products. [1] and [2] represent the majority of approved claims. This table collected all the published approved Article 13.1 Claims from newest to oldest.

Source: EFSA website, October, 2009- August, 2012

3.3.2 Article 13.5 claims

In total 15 Article 13.5 claims have been assessed with favorable outcomes. However, five out of fifteen are resubmitted claims. Thus the Table 3-3 below only shows 11 first-time submission claims with favorable outcomes.

Table 3-3: Article 13.5 approved claims published by EFSA

Products/components	Function of claims	Countries
Hydroxyanthracene derivatives	improvement of bowel function	France
Glycaemic carbohydrates	recovery of normal muscle function	France

"Non-fermentable" carbohydrates	maintenance of tooth mineralization by decreasing tooth demineralization	France
Monacolin K in SYLVAN BIO red yeast rice	maintenance of normal blood LDL-cholesterol concentrations	Netherlands
Cocoa flavanols	maintenance of normal endothelium-dependent vasodilation	Belgium
Glucose	contribution to energy-yielding metabolism	Germany
Sugar beet fiber	increasing fecal bulk	Denmark
Slowly digestible starch in starch-containing foods	reduction of post-prandial glycemic responses	Belgium
L-tyrosine	contribution to normal synthesis of dopamine	UK
"Tooth kind" drinks	reduction of tooth demineralization	UK
Water-soluble tomato concentrate (WSTC I and II)	platelet aggregation	UK

Source: EFSA website, October, 2009- August, 2012

3.3.3 Article 14 claims

Table 3-4 shows that in total 32 submitted Article 14 claims have had favorable outcome. Fifteen submitted protocols are from France, which means that among the approved claims French manufactures had a larger chance of being approved by NDA panel than those of other countries.

Table 3-4: Article 14 approved claims published by EFSA

Products/ components	**Functions**	**Countries**
Magnesium	contribution to normal development of bone	France
Caffeoylquinic acids, monacolin K, policosanols, OPC, allicin, d-α-tocopheryl hydrogen succinate, riboflavin and inositol hexanicotinatein	reduction of blood LDL-cholesterol concentrations	France
Increasing maternal folate status by supplemental folate intake	reduced risk of neural tube defects	UK
Vitamin A	contribution to normal development and function of the immune system	France

Iron	contribution to normal cognitive development	France
3 g/day plant stanols as plant stanol esters	lowering blood LDL-cholesterol and reduced risk of (coronary) heart disease	Finland
Barley beta-glucans	lowering of blood cholesterol and reduced risk of (coronary) heart disease	Slovenia
Barley beta-glucans	lowering of blood cholesterol and reduced risk of (coronary) heart disease	Belgium
Vitamin D	risk of falling	Switzerland
Omega-3 fatty acids	reduction of LDL-cholesterol concentrations	France
Alpha-linolenic acid	contribution to brain and nerve tissue development	Germany
Thiamin	maintenance of normal neurological development and function	Germany
Oat beta-glucan	reduced risk of (coronary) heart disease	Switzerland
Sugar-free chewing gum	reduces the risk of dental caries	Germany
Sugar-free chewing gum and neutralisation of plaque acids	reduces the risk of dental caries	Germany
Thiamine and carbohydrate	energy-yielding metabolism	Belgium
Iron	cognitive development of children	France
Iodine	growth of children	France
Calcium plus Vitamin D3 chewing tablets	reduction of the risk of osteoporotic fractures by reducing bone loss	Germany
Low fat fermented milk	reduced risk of (coronary) heart disease	France
ALA	brain development	France
Lipil®	visual development	France
Enfamil® Premium	visual development	France
DHA & ARA	visual development	France
Dairy fresh cheese	bone growth	Spain
Animal protein	bone growth	France
Plant stanol esters	blood cholesterol	UK
Vitamin D	bone growth	France
Calcium	bone growth	France
Calcium and vitamin D	bone strength	UK
Plant sterols	ower/reduced blood cholesterol and reduced risk of (coronary) heart disease	Netherlands

ALA and LA	growth and development of children	Netherlands

Source: EFSA website, October, 2009- August, 2012

3.4 Result

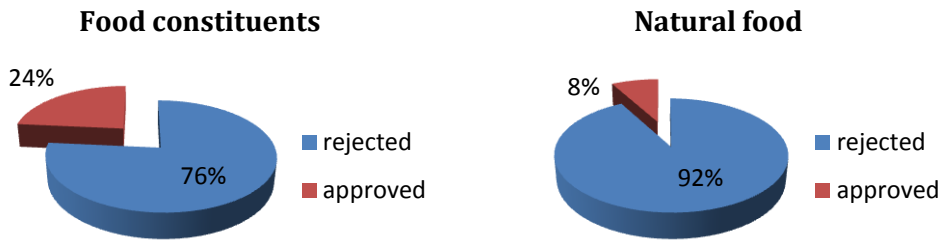
3.4.1 Analysis of approval rate via pie charts: Article 13.1 claims

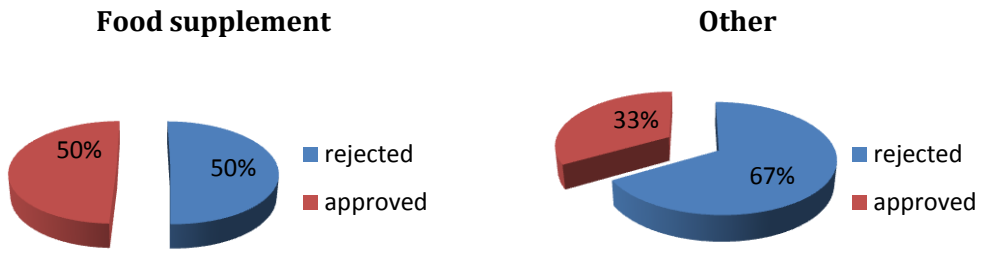
The general overview on percentage of approved claims conditional on each feature has been illustrated using pie charts from Excel. Pie charts are conducted in the five major groups of factors: 1) food categories group 2) food ingredients group, 3) function group, 4) submitted study group, 5) re-submitted protocol group. In each group the percentage of approval and rejection of each feature will be shown.

The pie chart is made using the number of approved and rejected protocols, as well as total protocols with each feature considered. For example 221 claims have been re-submitted by the manufactures, among which there are 136 rejected and 85 approved. The pie chart will give a representation of the approval and rejection rate of re-submitted claims:

(Approved claims/ total number of claims) * 100%

Figure 3-1: Percentage of positive and negative EFSA opinions by food categories of Article 13.1

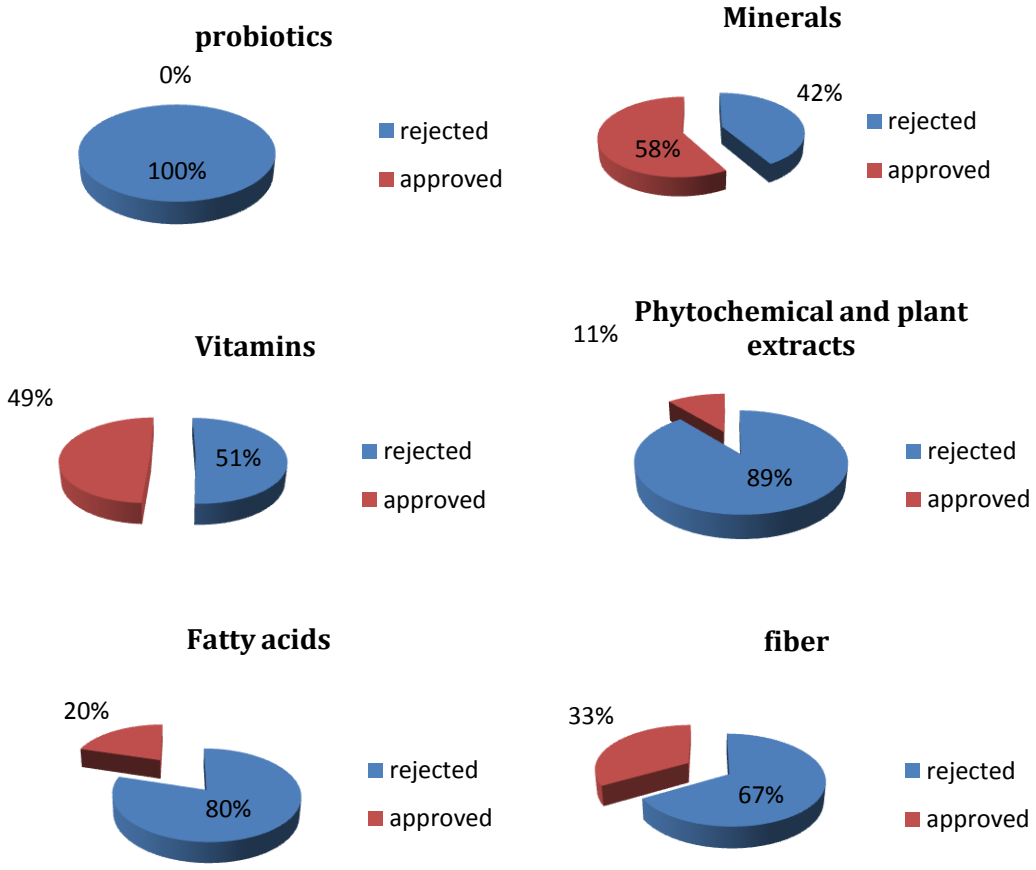


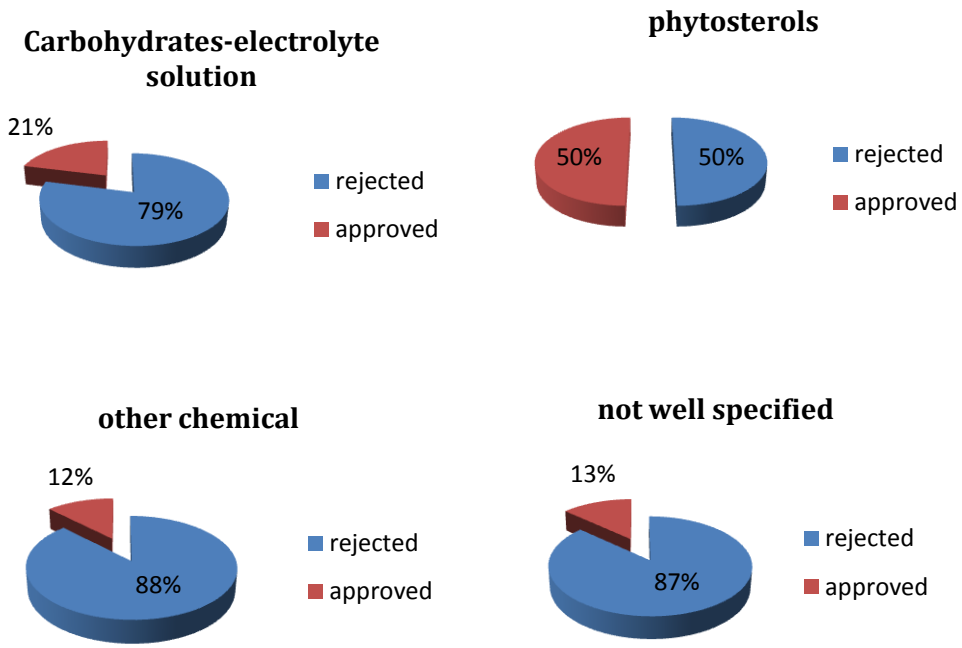


Source: EFSA website, October, 2009- August, 2012

The rejection rate of natural foods is 92 per cent, which means only few natural food have been approved. The food supplement has the highest approval rates of 50 per cent of the claims being approved.

Figure 3-2: Percentage of positive and negative EFSA opinions by food ingredients of Article 13.1



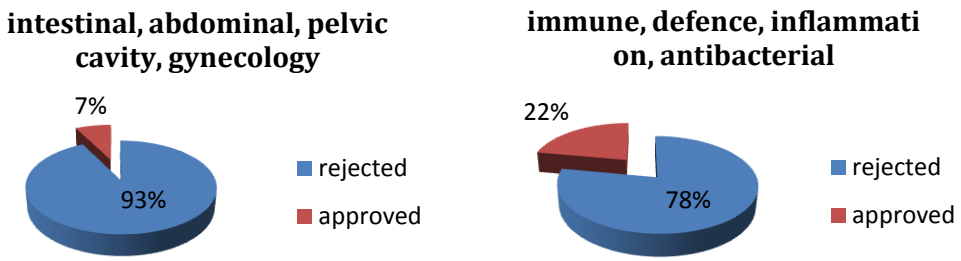


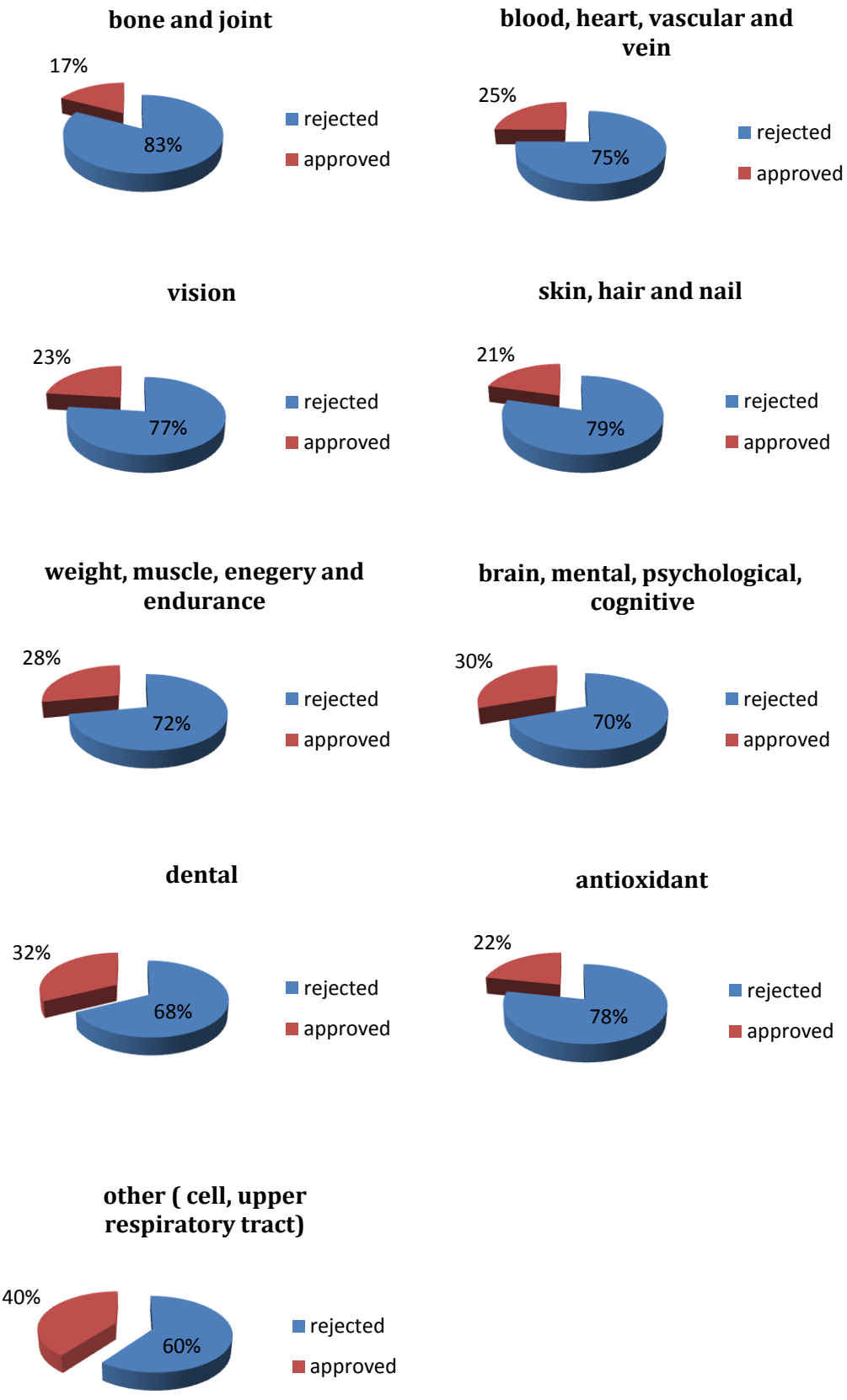
Source: EFSA website, October, 2009- August, 2012

The rejection rate of probiotics claims is 100 per cent, which means no probiotics claims have been approved.

The mineral has the highest approval rates, 58 per cent of the claims have been approved. Vitamin and phytosterols have the second largest approval rate, which accounts for circa 50 per cent. The percentage of approval for the other four food ingredient/compounds (phytochemical and plant extraction, fiber, fatty acids and carbohydrates-electrolyte solution) are lower than 35 per cent.

Figure 3-3: Percentage of positive and negative EFSA opinions by function claims of Article 13.1

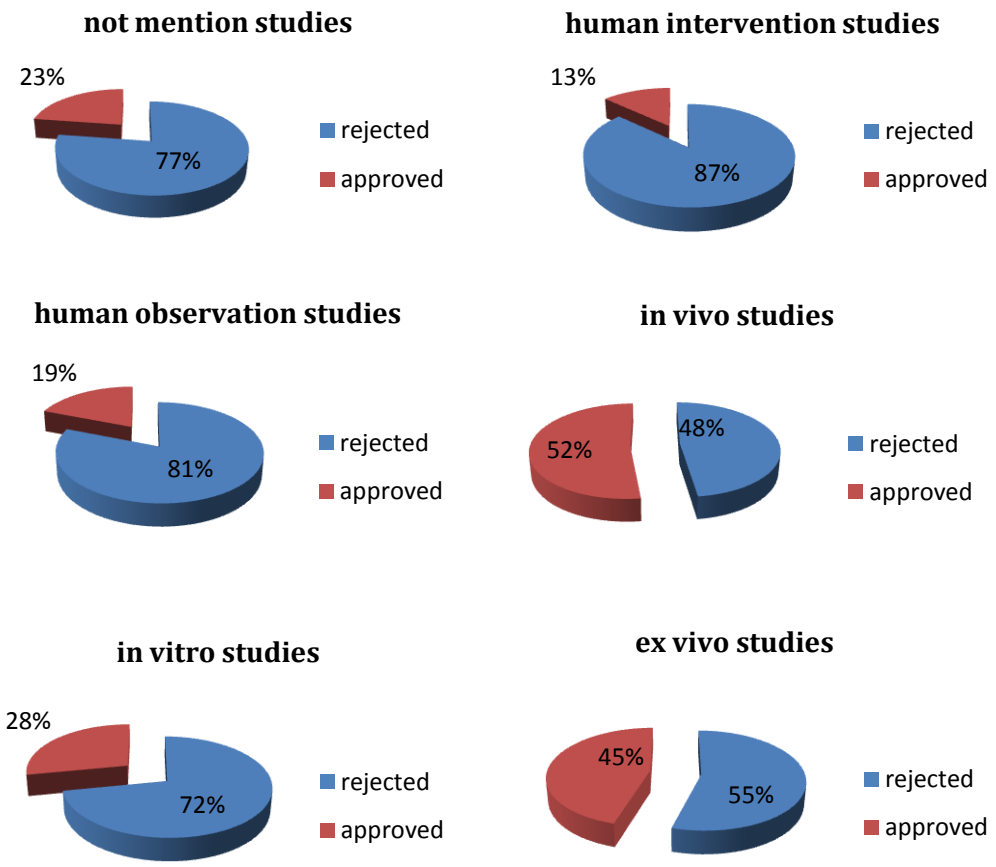


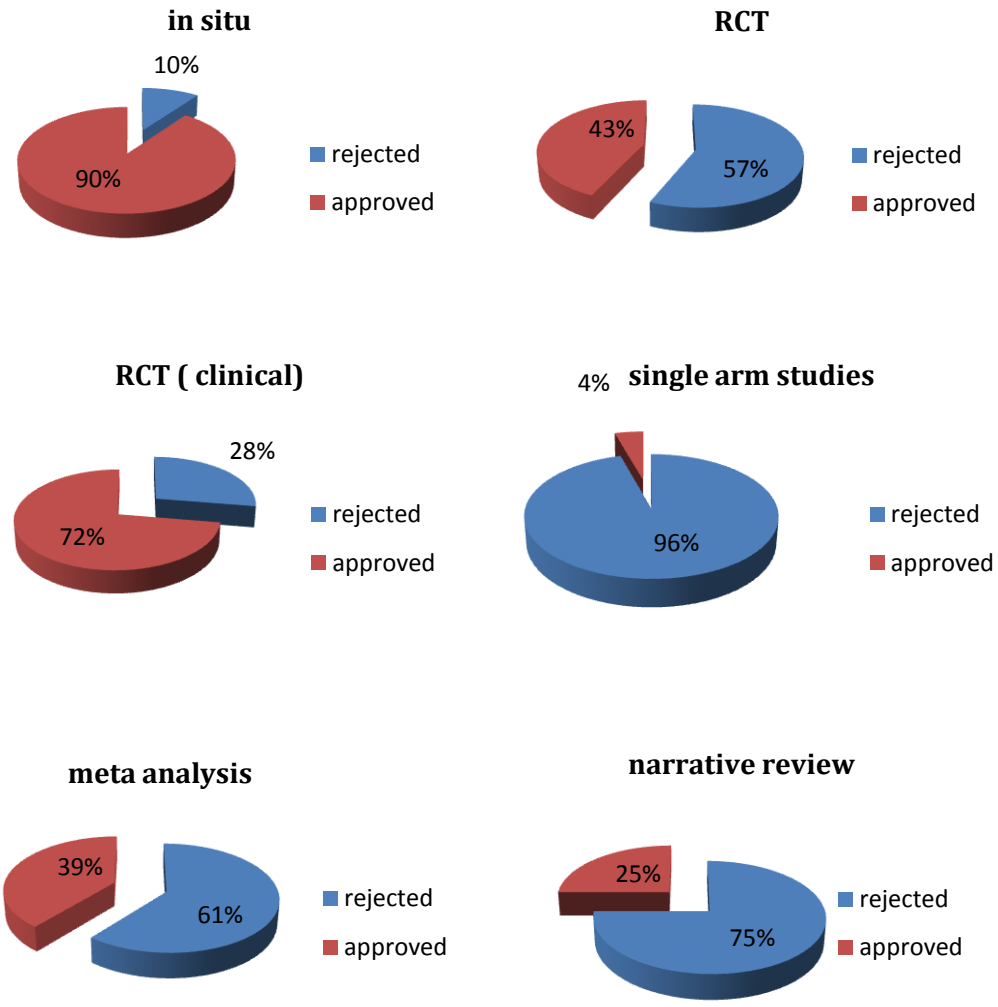


Source: EFSA website, October, 2009- August, 2012

The dental and brain reach the peak with the 32 and 30 per cent of claims being approved, respectively. However, the intestinal health claims have the lowest probability of approval, which is 7 per cent. In total 121 submitted claims are related to intestinal, of which 20 submitted claims are phytochemical compounds and have all been rejected. Meanwhile, 43 of 121 submitted claims are for probiotics compounds, and have all been rejected as well. This can be interpreted that one-third of the rejected claims of intestinal has compounds of probiotics. The probiotics could be one of the major reasons to reduce the percentage of approval for intestinal. For the rest majority organs affected by the healthy, there are 17 to 28 per cent of claims have a favorable outcome. If manufactures submit claims related to the dental and brain functions, they will have roughly a 30-per-cent chance to be approved by NDA panel. The approval rate of submitting intestinal claims is 7 per cent. Thus manufactures are suggested not to summit intestinal claims.

Figure 3-4: Percentage of positive and negative EFSA opinions by submitted studies of Article 13.1





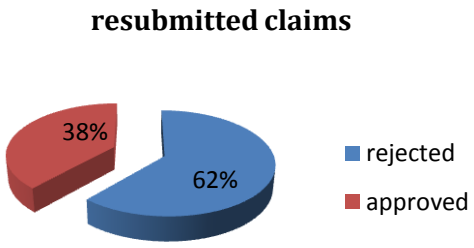
Source: EFSA website, October, 2009- August, 2012

Figure 3-4 illustrates the approval rates of Article 13.1 on studies submitted to the NDA panel. Below we assess the approval rate of claims conditional to the types of submitted studies used to prove the relationship of the products/constituents and the certain functions.

Surprisingly claims with in situ studies have 90 per cent approval rates, which mean that manufactures having submitted claims by conducting in situ studies, in 90 per cent of the cases applications had favorable outcomes. The type of study submitted with second highest approval rates is for submissions with RCT clinical trials, which have approval rates of 72 per cent. Moreover, the approval rates of claims carrying the other four types of scientific studies are: 39 per cent for meta analysis, 43 per cent for RCT, 45 per cent for ex vivo studies and 52 per cent in vivo studies. However, submitting single arm study only has a 7-per-cent chance to be approved, which is the lowest approval rate among

the 12 types of studies. The percentage of approval for the others is circa 20 per cent. Based on the pie charts above, submitting protocols with in situ, and RCT clinical may increase the probability of approval, while submitting single arm studies will decrease the probability of approval.

Figure 3-5: Percentage of positive and negative EFSA opinions by re-submitted claims of Article 13.1



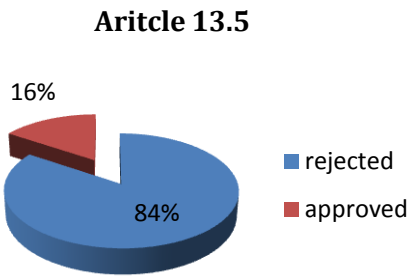
Source: EFSA website, October, 2009- August, 2012

From the pie chart in Figure 3-5, 62 per cent of re-submitted Article 13.1 claims have been rejected. Based on the pie chart, if manufactures do not receive a positive outcome for the first-time submission, their re-submitted protocols will still have a large chance to be rejected by the NDA panel. Thus the manufactures may not learn from the scientific opinions for their first failed submission. One of the reasons might be that the scientific opinions from EFSA are not useful (for example a pure scientific opinion instead of a specific guideline toward success) for manufactures to increase their approval rates.

3.4.2 Analysis of approval rate via pie charts: Articles 13.5 and Article 14 claims

The general overview on approval rate claims conditional on each factor has been analyzed using pie charts as well. Pie charts are conducted in the seven major groups of features; 1) type of claims group, 2) food categories group, 3) food ingredients group 4) function group, 5) submitted studies group, 6) countries group (countries/city that manufactures come from), 7) re-submitted protocol group.

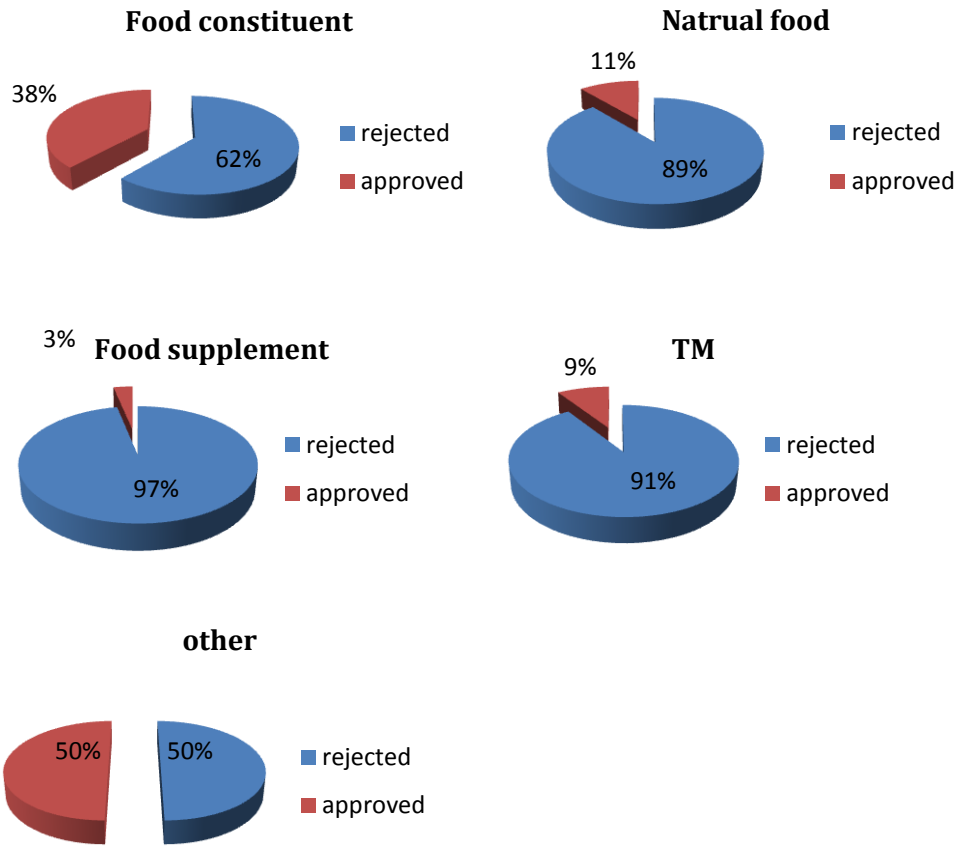
Figure 3-6: Percentage of positive and negative EFSA opinions by type of claims of Article 13.5 and Article 14 claims



Source: EFSA website, October, 2009 - Jan, 2014

From the pie chart in Figure 3-6, 84 per cent of Article 13.5 claims have been rejected. In other words, the Article 14 claims have a higher approval rate than Article 13.5 claims.

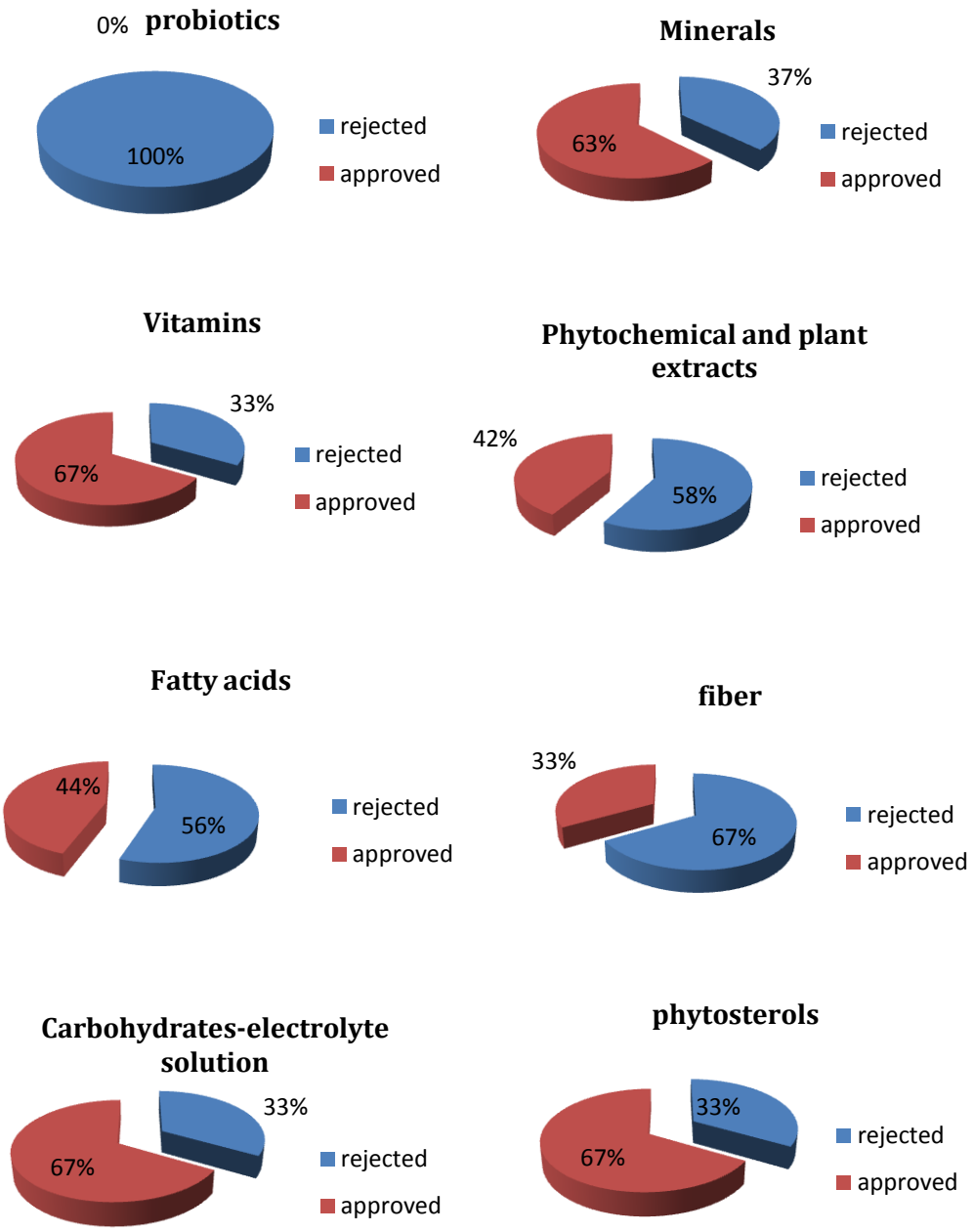
Figure 3-7: percentage of positive and negative EFSA opinions by food categories of Article 13.5 and Article 14 claims

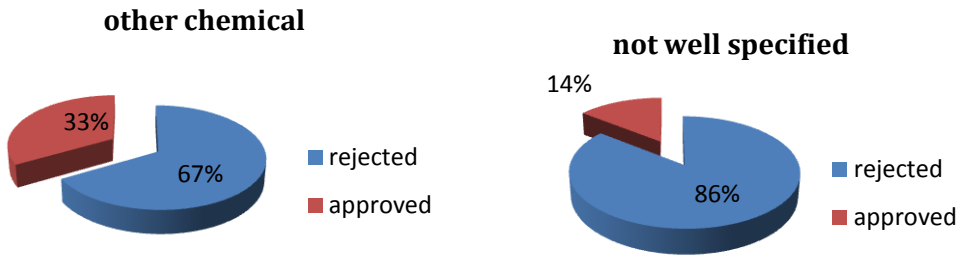


Source: EFSA website, October, 2009 - Jan, 2014

In Figure 3-7, factors of food supplement has a 97-per-cent chance to be rejected. TM and register with 91 per cent claims have been rejected.

Figure 3-8: percentage of positive and negative EFSA opinions by food ingredients of Article 13.5 and Article 14 claims

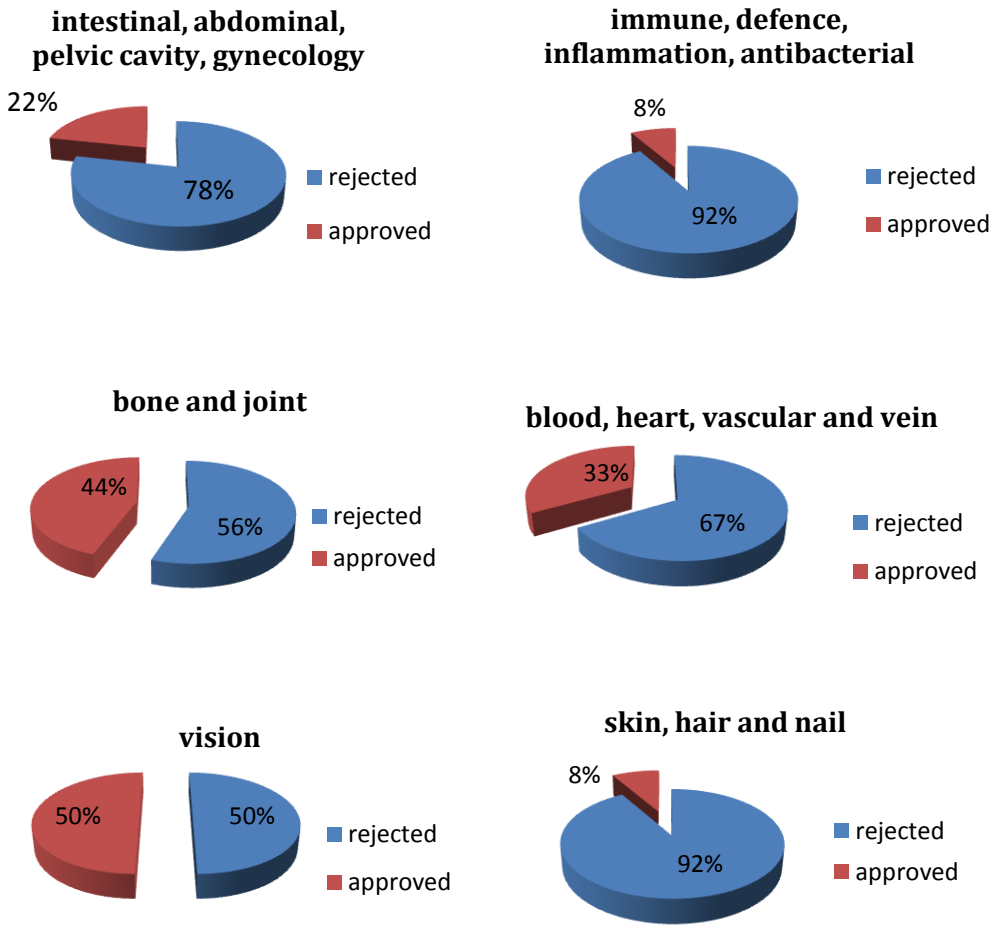


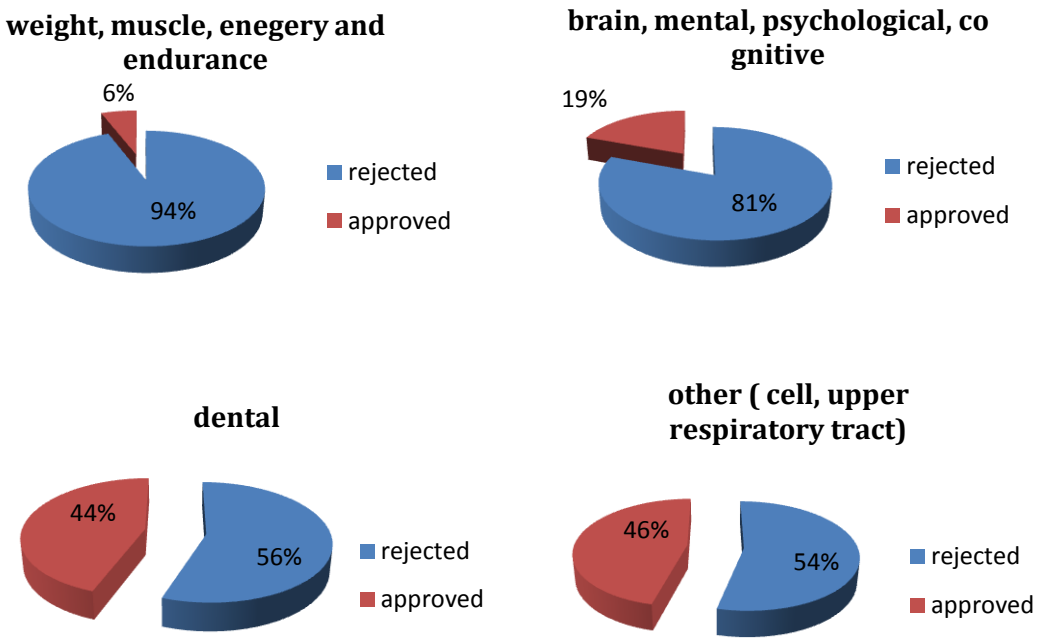


Source: EFSA website, October, 2009 - Jan, 2014

100 per cent of probiotics and 86 per cent of not well specified claims have been rejected by the NDA panel. The mineral, vitamin, phytosterols and carbohydrates-electrolyte solution have circa 65 per cent approval rates, which occupy the largest approval rates among group of food ingredients.

Figure 3-9: Percentage of positive and negative EFSA opinions by function claims of Article 13.5 and Article 14

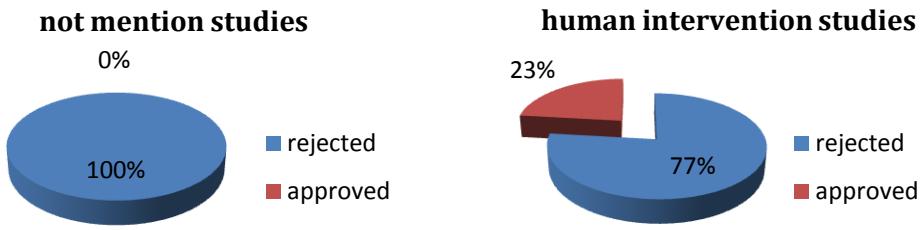


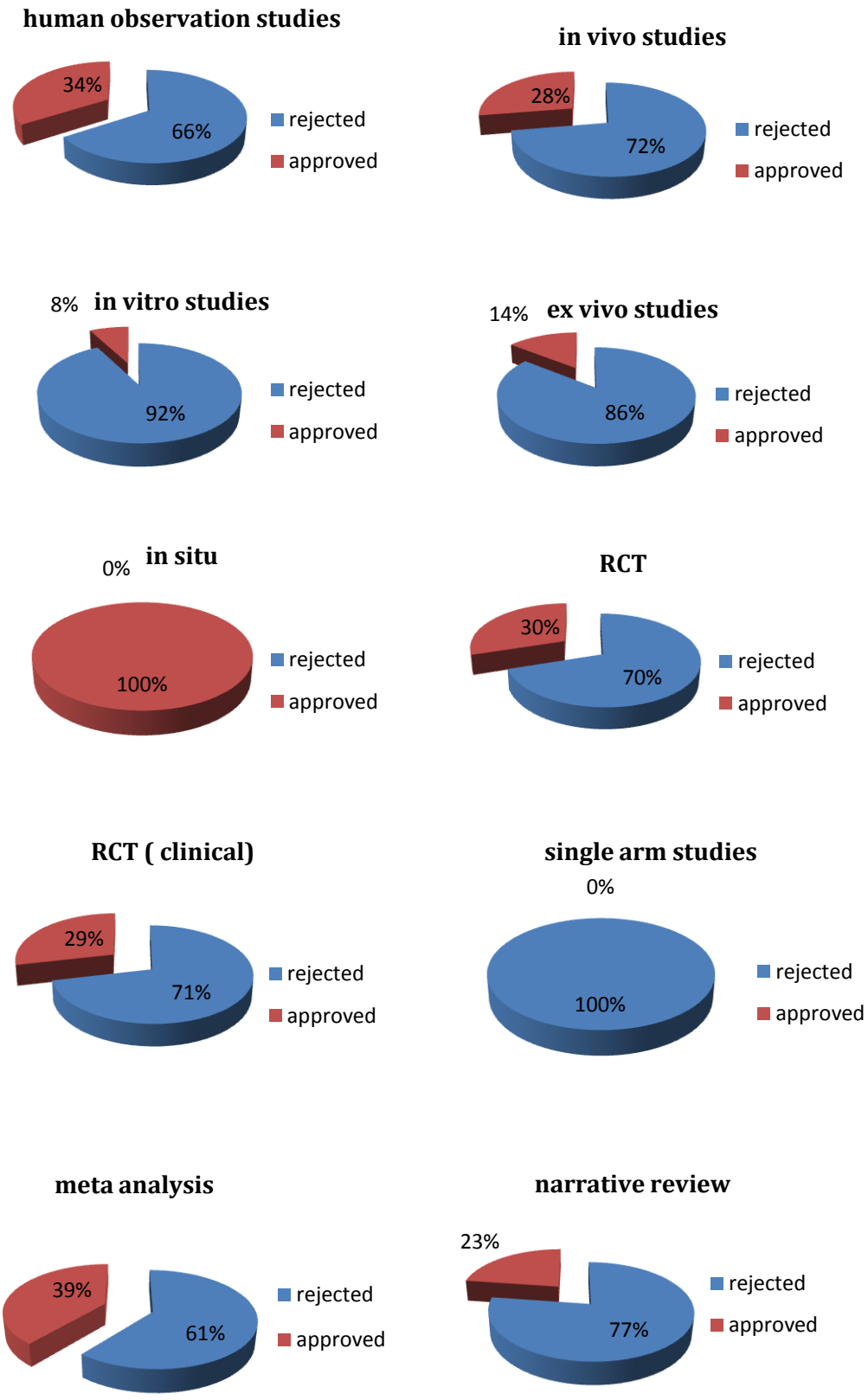


Source: EFSA website, October, 2009- August, 2012

In Figure 3-9, 80 per cent of the protocols related to intestinal, immune, skin and hair, weight and muscle, and brain and mental are rejected. The weight and muscle have 94 per cent claims being rejected, which is the highest rejection rate among all the organs. For the remaining organs of bone and joint, vision, dental and others, around half of the claims will have a favorable outcome. So manufactures are not suggested to submit protocols related to the function of intestinal, immune, skin and hair, weight and muscle, and brain and metal since those five features are hardly to be assessed with favorable outcomes.

Figure 3-10: Percentage of positive and negative EFSA opinions by submitted studies of Article 13.5 and Article 14



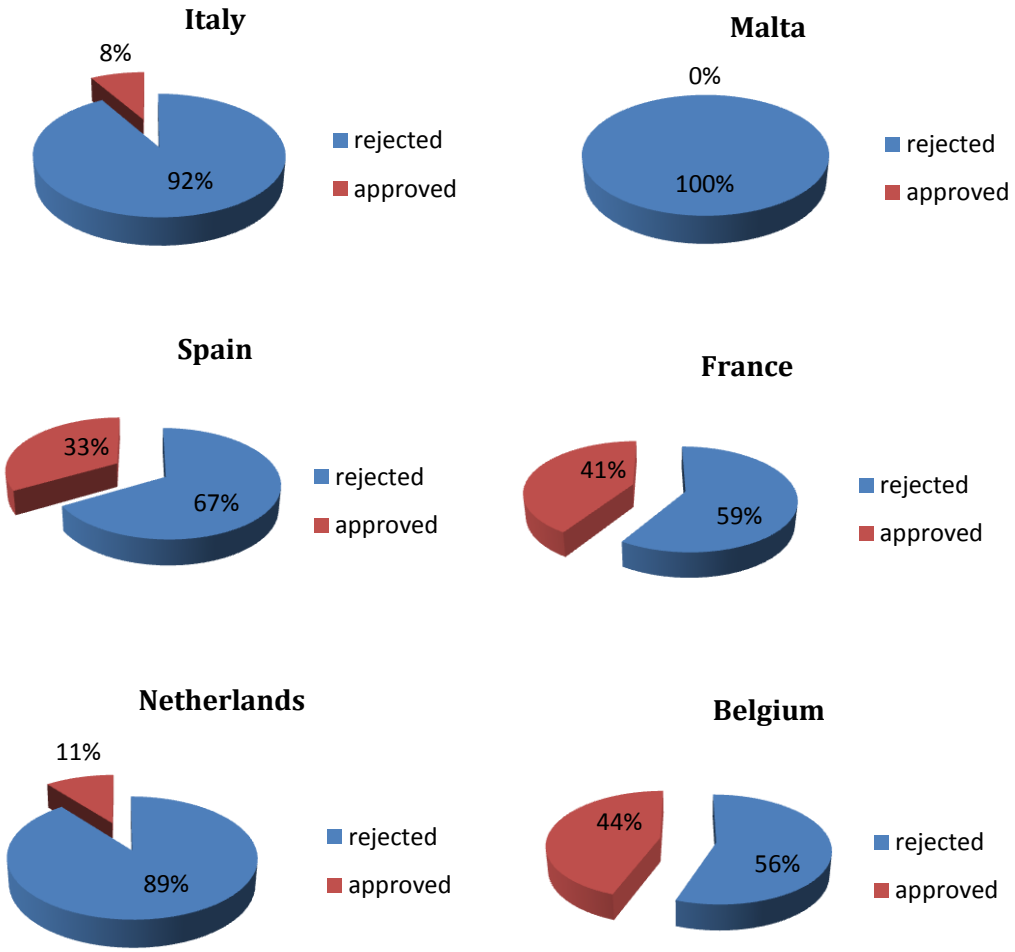


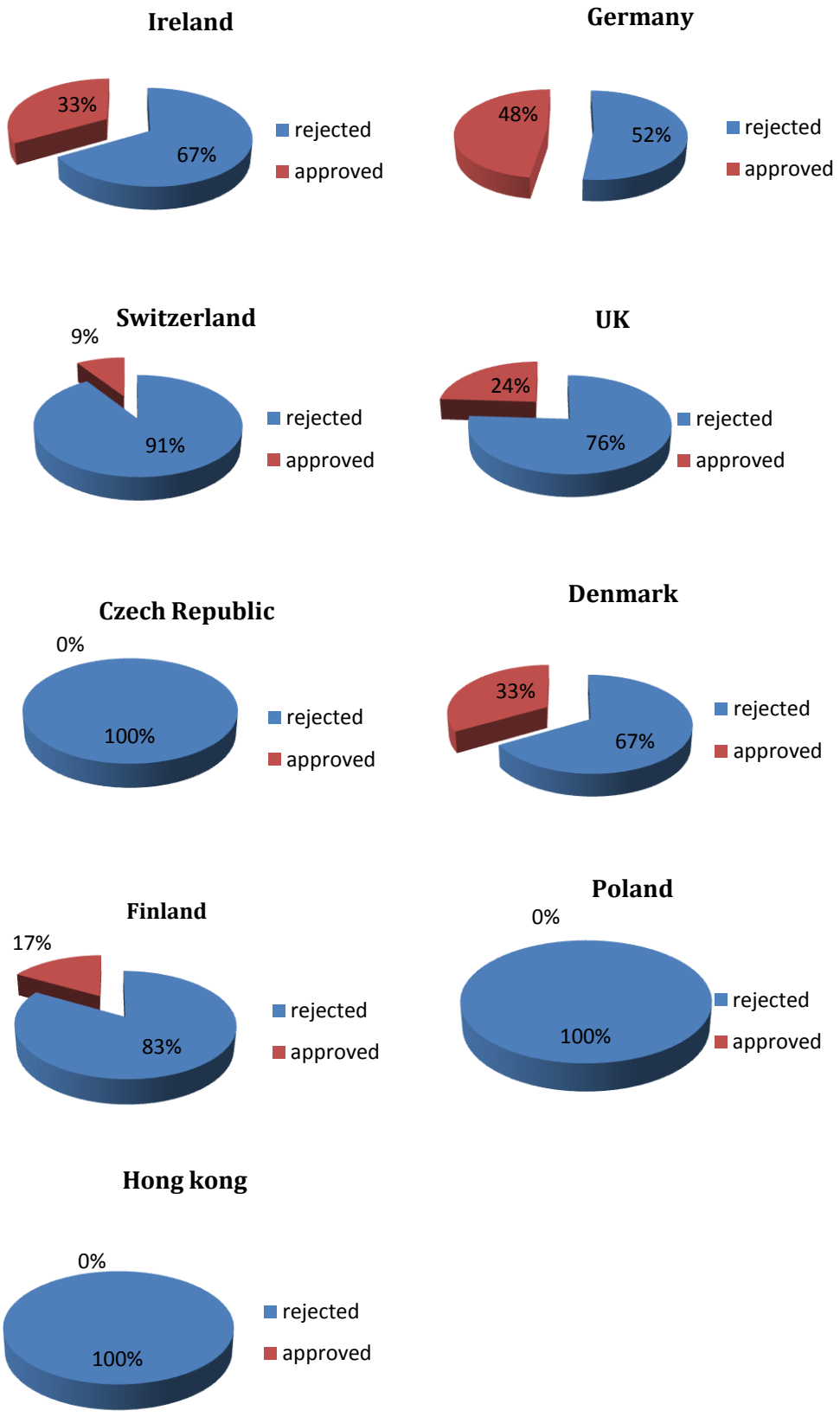
Source: EFSA website, October, 2009- August, 2012

Figure 3-10 illustrates the rate of positive and negative opinions of Article 13.5 and

Article 14 claims conditional on the types of studies submitted. It can be seen that all the claims using single arm studies and claims without submitting any studies have negative opinions. Although claims supported by in situ studies have 100 per cent of approval rates, it is still worth to mention that there is only one application submitting in situ studies (in the appendix). So the result of in situ studies is not representative. Protocols submitted with evidence from meta-analysis have a 39 per cent of approval rate. The percentage of approval for the other types of studies ranges from 14 per cent to 34 per cent. Based on the pie charts above, manufactures are recommended to submit meta-analysis compared with other studies. Manufactures are suggested not to submit any studies as well as single arm studies.

Figure 3-11: Percentage of positive and negative EFSA opinions by countries of Article 13.5 and Article 14

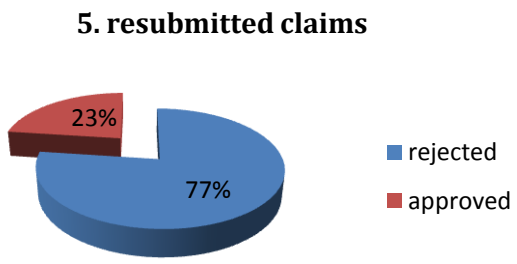




Source: EFSA website, October, 2009- August, 2012

Figure 3-11 illustrates the positive and negative opinions of Article 13.5 and Article 14 claims for claims submitted by manufacturers in different countries. In 7 countries (Hungary, Slovenia, United Arab Emirates, Japan, Israel, Estonia and Sweden) only one manufacturer submitted protocols; and for these 7 countries the results are not representative. Therefore the pie charts in Table 3-6 only present claims which were submitted from 15 countries/cities. The claims submitted from Malta, Czech Republic, Poland and Hong Kong were all rejected. The protocols submitted from France, Belgium and Germany were approved with a chance of circa 40 per cent.

Figure 3-12: Percentage of positive and negative EFSA opinions by re-submitted protocols of Article 13.5 and Article 14



Source: EFSA website, October, 2009- August, 2012

From the pie chart in Figure 3-12, 77 per cent of re-submitted claims have been rejected. The number of failure claims is more than three times higher than that of the approved claims. We can conclude that the re-submission protocol process provided by EFSA will not help manufactures to improve their chances of approval. The transparency problem of the EFSA might be one of the most important reasons that re-submitted claims have relatively low approval rates.

3.4.3 Difference of approval rates across health claims

Table 3-5: Percentage of highest positive and negative opinions for submitting protocols of Article 13.1, Article 13.5 and Article 14 claims published by EFSA (source: EFSA website, October, 2009- August, 2012)

	Article 13.1 claims		Article 13.5 and Article 14 claims	
	Approval	Rejection	Approval	Rejection
Food ingredients	Mineral 58%	Probiotics 100%	Vitamin 67%	Probiotics 100%
Functions	Others 40%	Intestinal 93%	Vision 50%	Weight and muscle 94%

Submit studies	In situ 90%	Single arm 96%	Meta-analysis 39%	Single arm and not mention studies 100%
Countries	No	No	Germany 48%	Malta, Poland, Hong Kong and Czech 100%
Re submitted claims	38%	62%	23%	77%

Table 3-5 shows the difference of highest approval and rejection rates on health claims among the five groups of factors. In the food ingredients group, 58 per cent of mineral have been approved for Article 13.1 claims, 67 per cent of vitamin protocols have been approved for Article 13.5 and 14 claims. Those two products/ingredients show the highest favorable outcome rates among food ingredients for health claims. However, the probiotics have a 100 per cent rejection probability in both Article 13.1 claims and combination of Article 13.5 and Article 14 claims. My result on the probiotics is same with the studies from Guarner (2011) and Van Loveren (2012). They indicated that probiotics published by EFSA have not been favorable. Moreover, 100 per cent of rejection probability of probiotics claims had been shown in the study of Valls' (2013).

Submitting protocols of in situ studies will have the highest favorable outcome of 90 per cent for Article 13.1. Meta-analysis has 39 per cent approval rate for Article 13.5 and Article 14 claims, which is highest in the submitted studies group. However, submitting single arm studies in Article 13.1 claims will have a 96-per-cent chance to be approved and in Article 13.5 and Article 14 claims the percentage of approval is 100 per cent. The percentage of approval for countries group is not available for Article 13.1 claims, because there is no information about companies provided for Article 13.1 claims. There is a 62-per-cent chance that resubmitted claims receive negative opinions for Article 13.1 claims, 77 per cent for Article 13.5 and Article 14 claims. It means manufactures may not have larger chances to be approved by EFSA for their re-submissions than the first-time submissions. In other words, the re-submission process provided by EFSA will not help manufactures to increase the approval rate for their multiple submissions. The studies of both Borras (2007) and Vero (2012) also indicated that the EFSA faces the transparency issues.

Each of the eight factors (in situ, Hungary, Slovenia, United Arab Emirates, Japan, Israel, Estonia and Sweden) has one protocol submitted (see Figure 3-7 to Figure 3-9). Although those 8 factors have been illustrated using pie charts, they are not representative for the approval rates for Article 13.5 and Article 14 claims.

4. Discussion

We performed a preliminary description for the approval rate of health claims (Article 13.1 claims and combination of Article 13.5 and Article 14 claims). Valls (2013) analyzed the influence of 8 most popular ingredients on the combination of all health claims and his study indicates that products such as phytosterols, carbohydrate-electrolyte solutions, vitamins and minerals have high rates of approval. However, products such as probiotics, fiber and phytochemicals have been considered as negative indicators on increasing the approval rates for health claims.

The results of this thesis shows that Article 13.1 claims, vitamins, minerals and phytosterols have a higher approval rate of health claims. However, the carbohydrate-electrolyte solution only shows 21 per cent probability of approval, which differs from the results of Valls. Meanwhile, claims based on vitamins, phytosterols, carbohydrates-electrolyte solution and minerals are more likely to be approved for Article 13.5 and Article 14 claims. This result is exactly the same as Valls'. Moreover, probiotics, phytochemicals, fatty acids and carbohydrates-electrolyte solution have negative impacts on improving the approval rate for Article 13.1 claims. Fiber only has probability of 33 per cent to be approved for Article 13.1 claims. For Article 13.5 and Article 14 claims, probiotics, fiber, phytochemical and fatty acid are less likely to be approved; this result is almost the same as Valls'.

As for probiotics, both Article 13.1 claims and combination of Article 13.5 and Article 14 claims show 100 per cent rejections. The studies of Guarner (2011), Van Loveren (2012) and Valls (2013) also indicated the same results. So we can conclude until now there is no improvement on the approval rates of probiotics claims.

Both Borras (2007) and Vero (2012) concluded that the EFSA needs to improve the transparency issue. Based on the results of my study on the re-submitted protocols, 62 per cent of Article 13.1 claims and 77 per cent of combination of Article 13.5 claims and Article 14 claims have had unfavorable outcomes. Thus the low approval rate for submitting protocols are probably caused by the transparency issue deeply embedded in EFSA. The EFSA is suggested to open the assessment processes to increase the transparency (Borras, 2007; Vero 2012). Moreover, EFSA held a conference to enhance the transparency in 2013, which will result in revising a policy on openness and transparency to increase the transparency of EFSA. Based on the findings above, the transparency is still a problem for EFSA.

There are also some limitations in my study. The data of Article 13.1, Article 13.5 and Article 14 claims were collected from EFSA in January of 2014. Thus the results of this thesis may not be valid after five years or even early. Furthermore, the EFSA is trying to enhance their transparency. A policy on openness and transparency will be revised by 2014. After that, if EFSA solves the transparency issue successfully, the approval rate of the claims will increase significantly. At that time, the result of this study may not reliable anymore.

There are also some limitations in the data collection process. Some of the published scientific opinions do not mention the submitted studies and even the authors of the studies. Thus there is a factor named not well defined studies in the submitted study group (see master thesis). The final result might not be that perfect, when some of the studies are missing.

In the pie charts of Article 13.5 and Article 14 claims only one application has been submitted for each of eight factors: in situ, Hungary, Slovenia, United Arab Emirates, Japan, Israel, Estonia and Sweden. Thus the pie charts of those eight features are not representative for the approval rates for Article 13.5 and Article 14 claims.

5. Conclusion and Recommendation

This study provides a detailed background literature review for my Master thesis and graphical representations of the approval rates of health claims.

According to the results of Article 13.1 claims, 50% of food supplement, 58% of mineral, 49% of vitamin, 50% of phytosterol, 32% of dental, 30% of brain, 90% of in situ studies and 72% of RCT clinical trials have been approved. If a submitted protocol relates to food supplements or contains mineral, vitamin, phytosterol, dental, brain, in situ studies and RCT clinical trials is more likely to be approved by NDA panel. However 92% of natural food, 100% of probiotics, 93% of intestinal and 96% of single arm studies have been rejected. Thus submitted claims carrying products of natural food, probiotics, intestinal and single arm studies will result in unfavorable outcomes (to be rejected by NDA panel).

For results of Article 13.5 and Article 14, claims with vitamin, phytosterols, and carbohydrates-electrolyte solution show a 67 per cent approval rate; claims related to vision, bone and joint, dental shows circa 50 per cent of claims being approved; the percentage of approval for protocols with food constituents and meta-analysis is 39 per cent. Moreover, claims submitted by manufactures from Germany, Belgium or France have circa 45 per cent of claims approved. All protocols based on probiotics, where no studies were mentioned, single arm studies showed 100 per cent negative outcomes, and food supplement products showed 97 per cent of claims being rejected.

The approval rates of claims for intestinal health are lowest among Article 13.1, Article 13.5 and Article 14 claims. Thus manufactures are suggested not to submit protocols of intestinal products.

The approval rate of re-submitted protocols is 38 percent for Article 13.1 claims and 23 per cent for Article 13.5 and Article 14. Thus, the re-submission process provided by EFSA may not assist manufactures to improve their approval rates.

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Appendix

- Data of pie chart for Article 13.1 claims (four groups)

1. product/its constituent			
	rejection	approval	total
probiotics	68	0	68
Minerals	65	91	156
Vitamins	69	67	136
Phytochemical and plant extracts	155	19	174
Fatty acids	67	17	84
fiber	10	5	15
Carbohydrates-electrolyte solution	15	4	19
phytosterols	1	1	2
other chemical	163	23	186
not well specified	125	19	144

2. health claims			
	rejection	approval	total
intestinal, abdominal, pelvic cavity, gynecology	112	9	121
immune, defence, inflammation, antibacterial	53	15	68
bone and joint	43	9	52
blood, heart, vascular and vein	130	43	173
vision	20	6	26
skin, hair and nail	62	16	78
weight, muscle, enegery and endurance	108	42	150
brain, mental, psychological, cognitive	57	25	82
dental	21	10	31
antioxidant	36	10	46
other (cell, upper respiratory tract)	94	62	156

3. submit studies			
	rejection	approval	total
not mention studies	249	73	322
human intervention studies	287	43	330
human observation studies	17	4	21
in vivo studies	59	64	123
in vitro studies	192	75	267
ex vivo studies	18	15	33
in situ	2	18	20
RCT	72	55	127
RCT (clinical)	32	84	116
single arm studies	22	1	23
meta analysis	53	34	87
narrative review	3	1	4

	rejection	approval	total
4. resubmitted claims	136	85	221

- Data of pie chart of Article 13.5 and Article 14 claims (five groups)

1. Products/constituents			
	rejection	approval	total
probiotics	16	0	16
Minerals	3	5	8
Vitamins	4	8	12
Phytochemical and plant extracts	7	5	12
Fatty acids	5	4	9
fiber	2	1	3
Carbohydrates-electrolyte solution	1	2	3
phytosterols	2	4	6
TM	80	8	88
other chemical	16	8	24
not well specified	12	2	14

2. health claims	rejection	approval	total
intestinal, abdominal, pelvic cavity, gynecology	29	8	37
immune, defence, inflammation, antibacterial	11	1	12
bone and joint	10	8	18
blood, heart, vascular and vein	22	11	33
vision	3	3	6
skin, hair and nail	11	1	12
weight, muscle, enegery and endurance	16	1	17
brain, mental, psychological, cognitive	25	6	31
dental	5	4	9
other (cell, upper respiratory tract)	7	6	13

3. submit studies	rejection	approval	total
not mention studies	7	0	7
human intervention studies	96	29	125
human observation studies	29	15	44
in vivo studies	42	16	58
in vitro studies	48	4	52
ex vivo studies	6	1	7
in situ	0	1	1
RCT	35	15	50
RCT (clinical)	5	2	7
single arm studies	5	0	5
meta analysis	25	16	41
narrative review	51	15	66

4. countries	rejection	approval	total
Italy	11	1	12
Malta	3	0	3
Spain	2	1	3
France	23	16	39
Netherlands	17	2	19
Belgium	5	4	9
Ireland	2	1	3
Germany	12	11	23
Switzerland	20	2	22
UK	19	6	25
Czech Republic	3	0	3
Denmark	2	1	3
Finland	5	1	6
Poland	5	0	5
Hongkong	5	0	5

		rejection	approval	total
5. resubmitted claims		37	11	48