Food Science and Technology Research, **27** (2), 169–179, 2021

doi: 10.3136/fstr.27.169

https://jsfst.smoosy.atlas.jp

Review

The use of functional agricultural products in the functional food labeling system and its challenges after five years

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Received December 10, 2020 ; Accepted January 26, 2021

In 2015, the Consumer Affairs Agency of Japan launched a new food labeling system known as "Foods with Function Claims (FFC)." This system allows food businesses to independently evaluate the safety and scientific evidence for the food they sell and responsibly label its functionality. To date, the following amendments to the FFC guidelines have been made in relation to fresh foods: the addition of a statement that a portion of the recommended daily intake can be taken, simplification of registration materials, the development of a Q & A section, the inclusion of mild disease range in clinical trials, and clarification of the treatments of pharmaceutical ingredients. In addition, a new guideline for post-checking has been put into operation.

Keywords: foods with function claims, guideline, functional agricultural product

Introduction

In recent years, the population of Japan has been declining, skewing toward a "super-aging" society (Arai *et al.*, 2015; [i]). The number of patients with lifestyle-related diseases continues to increase (Nakashini *et al*., 2004; Yamamoto *et al.*, 2003; Kanauchi *et al.,* 2004), and diseases associated with the aging population such as dementia (Makizako, 2017; [ii]) are also on the rise, resulting in an increase in national medical care expenditures exceeding 43 trillion yen in 2017 [(iii)]. These diseases are said to be largely caused by poor diet and lack of exercise, and the health issues surrounding food have become a major focus of attention. On the other hand, as the phrase "Food is Medicine - Eating healthy prevents and cures disease," or "ISHOKUDOUGEN" in Japanese suggests, food plays a major role in the maintenance and promotion of health and disease prevention. Research on the functionality of agricultural and food products indicates that the best functional foods are created through the screening, identification, and analysis of functional ingredients, analysis of mechanism of action, and development of agricultural products rich in these functional ingredients. Functional foods include dietary fiber, polyphenols, carotenoids, and other molecules, and verification through human trials (cohort studies and other observational and interventional studies) is essential to determine whether these foods contribute to health.

The Framingham Heart Disease Cohort (Taso and Vasan, 2015; McKeown *et al*., 2010; Wang *et al*., 2014), which began in 1948 in the USA, found that continuous intake of fruits and vegetables reduced the risk of stroke; the Seven Countries Cohort, which began in 1957, found that the Mediterranean diet, which was a diet high in monounsaturated fatty acids (olive oil), tomatoes, fish, and whole wheat grains, reduced the risk of stroke (Guasch-Ferré *et al*., 2014; Widmer *et al*., 2015; Tong *et al*., 2016) the Osaki cohort, which began in 2007 in Japan, found that dietary soy products, fish, seaweed, vegetables, fruits, and green tea reduced the risk of cardiovascular disease (Kuriyama *et al.*, 2006), and that continuous consumption of green tea reduced the risk of

Abbreviations: CAA, Consumer Affairs Agency; FOSDU, Foods for Special Dietary Uses; FHCs, Foods with Health Claims; FOSHU, Foods for Specified Health Uses; FNFC, Foods with Nutrient Function; FFC, Foods with Function Claims

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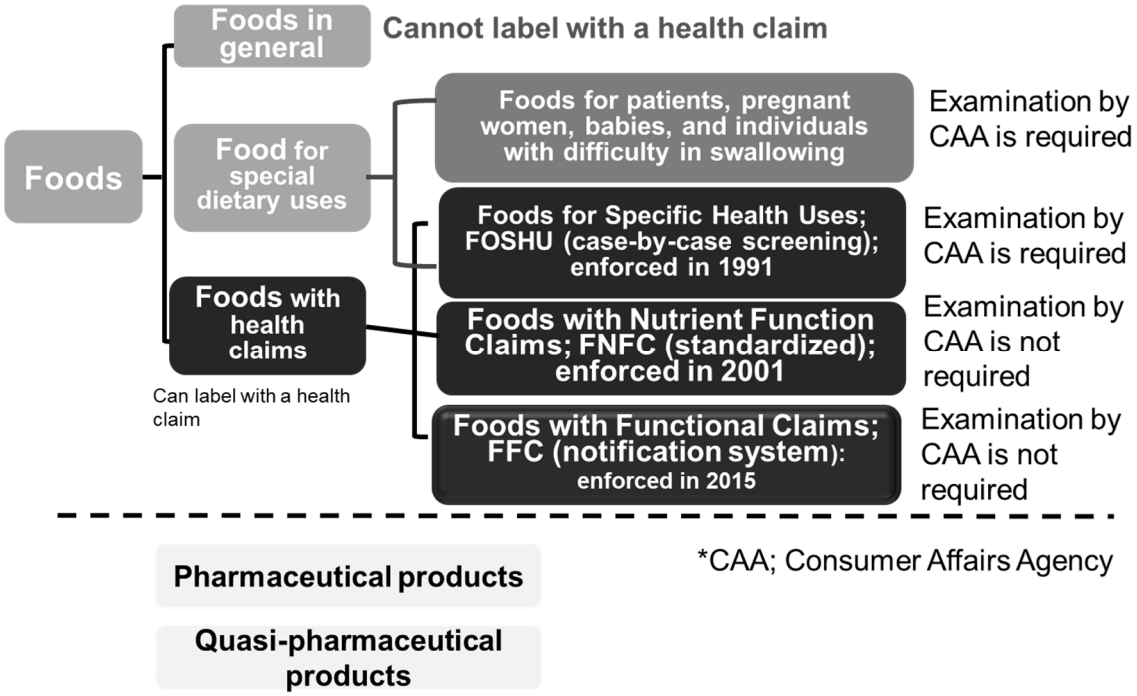

Fig. 1. Classification of orally ingested products in Japan

dementia in the elderly (Tomata *et al.*, 2012; Tomata *et al.*, 2016). Thus, the relationship between diet and health has been associated with reduced risk of disease onset. These findings have been utilized for the formulation of health guidelines in various countries.

Currently, there are three types of food labeling systems in Japan under which health claim can be labeled [(iv)]: the Food for Specified Health Use (FOSHU) system [(v)], the Food with Nutrient Function Claims (FNFC) system, and the Foods with Function Claims (FFC) system [(vi,vii)] (Fig. 1). The FFC system began on April 1, 2015, and allows businesses to voluntarily label their products with functionality under their own recognizance. This paper reviews its use in fresh food, as well as challenges of its revised guidelines.

Food function labeling system

Figure 1 shows the classification of products taken orally. In Japan, products taken orally are classified into two categories, food and medicines; all non-pharmaceutical products are considered to be food. The Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT) began conducting specific research on the functions of food products in 1984 (Shimizu, 2005), leading to the introduction of the Food for Specified Health Uses (FOSHU) in 1991, the first system in the world to allow food products to be labeled with their functions. Under the FOSHU system, each product was required to undergo a review for efficacy and safety, and the labeling had to be approved by the government.

Food with Nutrient Function Claims (FNFC), which has been in force since 2001, requires that a food be labeled with the amount of nutrients it contains as a percentage of recommended daily intake, including 13 vitamins (niacin, pantothenic acid, biotin, vitamin A, vitamin B1, vitamin B2, vitamin B6, vitamin B12, vitamin C, vitamin D, vitamin E, vitamin K, and folic acid), six minerals (zinc, calcium, iron, copper, magnesium, and potassium), and n-3 unsaturated fatty acids. The levels of these nutrients were required to be kept within the upper and lower limits specified.

The nutritional functions of some of these nutrients are as follows. (1) Zinc is a nutrient necessary for the normal function of taste. Zinc also helps to maintain the health of the skin and mucous membranes. Zinc is involved in the metabolism of proteins and nucleic acids, and helps maintain good overall health. (2) Vitamin C is a nutrient that helps maintain the health of the skin and mucous membranes, as well as having antioxidant properties. (3) Vitamin E is a nutrient that protects against lipid oxidation, and helps maintain cellular health through its antioxidant properties. (4) Folic acid is a nutrient that is important in the formation of red blood cells. Folic acid also contributes to the normal development of a fetus. (5) n-3 Unsaturated fatty acids help to maintain the health of the skin.

Since 2015, fresh food products have also been able to be labeled with this system. Such items currently labeled as fresh food include bell peppers (vitamin C), strawberries (vitamin C), bean saplings (folic acid), daikon radish (vitamin B12),

kumquat (vitamins C and E, and other ingredients), kiwi (vitamin C and E), and Petit Vert (folic acid and vitamin C), among others.

The CAA launched a new food labeling system, FFC, in April 2015. Under this system, companies and agricultural producers can independently evaluate and describe scientific evidence of health food benefits and functional properties to promote informed consumption. This labeling system differs from the FOSHU and FNFC criteria; FFC-labeled foods are presented to the Secretary-General of the CAA as products labeled with health claims based on scientific evidence, as assessed by food business operators (including food importers, manufacturers, producers, and retailers) (Maeda-Yamamoto, 2017; 2018). These "functional labeled foods" are foods for which companies and agricultural producers are responsible for labeling the functionality, based on scientific evidence, on their packaging. This system now requires declaration of products related to the maintenance and promotion of the health of both healthy and underserved individuals. Functional labeling of agricultural, forestry, and marine products and low-processed foods is also permitted. Unlike FOSHU, FFC allows labeling of functionality using body parts and subjective indicators of functionality. However, it is advisable to carefully check product label warnings and the information disclosed on the CAA website before purchasing and consuming these products. The function categories of FFC products are more numerous than those of FOSHU, and cover a wide range, including body fat, blood pressure, blood glucose, cholesterol, uric acid, liver, oral environment, stomach condition, eye and nose discomfort, urination, swelling, knee joints, sleep, physical fatigue, mental stress, cognitive function, skin moisturizer, eye focus, muscle function, and immune function (Table 1).

As of December 10, 2020, 3 550 products labeled according to the FFC guidelines (94 fresh foods, 1 658 processed foods, and 1 798 supplements) have been registered (Table 1). These include fresh foods such as Satsuma mandarin oranges (whose functional ingredient is β-cryptoxanthin, important for maintaining bone health), soybean sprouts (isoflavones, for maintaining bone health), apples (procyanidins, for reducing body fat), amberjack, yellowtail, sardines, see bream, eggs (DHA/EPA, for reducing blood lipids), rice, tomatoes, kale, paprika, enoki mushroom, soybean sprouts, grapes, bananas (gamma-aminobutyric acid (GABA); high blood pressure reduction), tomatoes (lycopene, which lowers LDL cholesterol), chili peppers (luteolin, which lowers blood sugar), spinach, kale (lutein, which maintains eye health), kale broccoli sprouts (sulforaphane glucosinolates, for enhanced ALT reduction), eggplant (acetylcholine, for enhanced blood pressure reduction), melon (GABA, for mental stress relief), chicken breast, pork carcass (imidazole dipeptide; memory maintenance, for fatigue reduction), pecan nuts (oleic acid, for LDL cholesterol reduction), bilberries (anthocyanins, for to maintain eye health), and sesame leaves (rosmarinic acid, for anti-allergic effects). They also include processed foods made from a single agricultural product, such as green tea (*O*-methylated catechin, to alleviate eye and nose discomfort caused by house dust), frozen spinach (lutein, to maintain eye health), steamed soybeans (isoflavones, for maintaining bone health), barley and steamed barley (β-glucan, for easing glucose absorption), no-wash rice (GABA, for regulating blood pressure), tomato juice (lycopene, for increasing HDL cholesterol), herring roe (DHA/EPA, for reducing triglycerides), agar (agar galactan, for regulating stomach condition), and Kawachi citrus juice (aurauptene, for improving cognitive function) (Table 2).

The promotion of the use of the FFC system for fresh food was noted in the Cabinet Office's Regulatory Reform Implementation Plan, approved by the Cabinet on June 9, 2017 (measures taken in 2018). The CAA and the Ministry of Agriculture, Forestry and Fisheries then discussed measures to promote the use of the FFC system for labeling fresh food. Based on this, in March 2018 and March 2019, the CAA published revised guidelines reflecting the distinctive treatment of fresh foods. In response to the Cabinet Office's suggestion, the National Agricultural Research Institute (NARO) has increased the systematic review freely available to businesses, and as of November 2020, green tea (functional ingredients: *O*-methylated catechin, epigallocatechin gallate), oranges (β-cryptoxanthin), apples (procyanidin), spinach (lutein), barley (β-glucan), soy (isoflavones), vegetables, mushrooms, and rice (GABA), tomatoes (lycopene), poultry (imidazole dipeptide, anserine), and fish (EPA/DHA) (Table 3) were published [(viii)]. In addition, vegetables (GABA, for stress relief) and purple sweet potato (anthocyanin, for liver protection) are slated to be published in the future. The systematic reviews have been used in 92 registrations to date.

It is also important to confirm the validity of the analytical method for functional ingredients prior to notification. In June 2017, the Japanese Agricultural Standards Law (JAS Law) was amended, and the JAS standard, which had been limited to the quality of goods (agricultural, forestry, and marine products and food) was expanded to include production methods (processes), handling methods (services, etc.), and testing methods for goods. With the expansion of the scope of the JAS standard, the current framework of certification was expanded, and a registration system was established to allow the Ministry of Agriculture, Forestry, and Fisheries to register testing organizations that complied with the international standards as registered testers.

Following this revision, methods of analysis of functional ingredients *O*-methylated catechin (JAS0002) [(ix)], β-

Table 1. Foods with function claims (1)

Category	Function claim	Functional ingredients
Visceral fat	reduces visceral fat and serum triglyceride	Lactoferrin, acetic acid, licorice glabridine, isoflavone from Ludzu flower, procyanidin, *Lactobacillus* (L) *gasseri* sp, gallic acid, EGCG, hydroxycitric acid, α-acids, and pcicose
Intestinal condition	・improves bowel movement ・maintains good digestion	Bifidobacterium, indigestible dextrin, inulin, *L. gasseri* sp, arabinoxylan, galactan, and guar gum
Blood pressure	maintains normal blood pressure	Lactotripeptide, α-linoleic acid, valyl-leucine, GABA, piperine, and valyl tirosine
Serum glucose	slows the elevation of postprandial serum glucose levels	Indigestible dextrin, barley β-glucan, salacinol, EGCG, calcium alginate, EGCG, chlorogenic acid, and iminosugar
Cholesterol	decreases LDL cholesterol levels	Barley β-glucan, lycopene, chitosan, α-linoleic acid, and hydrixytyrosol
Eye care	・supports the focus adjustment functions and conditions of eyes ・increases ocular pigment contents	Lutein, astaxanthin, cyanidin-3-glucoside, bilberry anthocyanin, and eriodictyol-6-C-glucoside
Allergy (eyes and nose)	alleviates feelings of discomfort in the eyes and/or the nose following exposure to house dust	*O*-Methylated catechin, caffeic acid, *L. acidophillus* L-92, *L. helveticus* SBT2171, rosmarinic acid, and soybean polysacchride
Skin	moisturizes skin and alleviates drying	Sodium hyaluronate, rice glucosylceramide, N-acetylglucosamine, rhodanthenone B, glucoraphanin, glycine-leucine, isoflavone, and astaxanthin
Muscle	maintains muscle mass and strength, improves walking ability	3-Hydroxy 3-methyl butyrate, milk sphingomyelin, 5,7-dimethoxylflavone, leucine, maslinic acid, and polymethoxyflavone
Urination	reduces the frequency of urination in women	Qunic acid
Swelling	reduce swelling in the face and legs	Lemon monoglucosyl hesperidin

Table 1. Foods with function claims (2)

Category	Function claim	Functional ingredients
Bone	maintains bone health by facilitating bone metabolism	β-Cryptoxanthin, soybean isoflavone, glucosamine, maltobionic acid, and collagen peptide
Knee	helps bending and stretching of knee joints	Collagen peptide, glucosamine hydrochloride, unmodified type II collagen, sodium hyaluronate, DHA, proteoglycan, and chondroitin sulfate
Peripheral body temperature	maintains peripheral temperature in cold seasons	Monoglucosyl hesperidin, ginger polyphenol, lactotripeptide, chlorogenic acid, and ellagic acid
Sleep	・supports healthy sleeping at night ・alleviates sleepiness or feelings of exhaustiveness while waking up	Theanine, serine, glycine, ornithine, GABA, crocetin,5-aminolevulinic acid, saracinol, isoquercitrin, S-allyl cysteine, proline-3- alkyl diketopiperazine, hyperoside, and safranal
Physical fatigue	reduces physical fatigue from normal daily activities	Imidazole dipeptide, coemzyme Q10, histidine, SOD, glucomoringin, paramylon, glycine, citric acid, and glucomolingin
Mental stress	relieves temporary mental stresses	GABA, theanine, crocin, *L. cassei* YIT9029, and SOD
Cognitive function	increases the accuracy of memory as a component of cognitive function	Gingko leaf flavonoid glycoside, gingko leaf terpene lactone, DHA, auraptene, and theanine, phosphatidylserine, plasmalogen, 6-methyl sulfinyl hexyl isothiocyanate, and bacopa saponin
Uric acid	reduces serum uric acid levels	Ampelopsin (dihydromyricetin), chitosan, anserine, polymethoxy flavone, luteolin, phytic acid, and PA-3 lactic acid bacteria
Liver	reduces serum GOT or GPT levels and maintains healthy liver function	Curcumin, bisacurone, and sulforaphane glucosinolate
Oral care	maintains good oral environment	*L. Rhamnosus 8020*, EGCG., and *Lactobacillus* LS1
Immune function	maintenance of immune function	*Lactococcus lactis* Plasma

Table 2. Examples of fresh food FFC and primary processing products FFC

Food items	Functional ingredients, recommended daily intake	Function claims
Satsuma mandarin	β-Cryptoxanthin, 3 mg	Maintaining bone health
Apple	Procyanidin, 110 mg	Reducing visceral fat
Grape	GABA, 12.3 mg	Maintaining normal blood pressure
Melon	GABA, 28 mg	Relieving temporary mental stress
Banana	GABA, 12.3 mg	Maintaining normal blood pressure
Bilberry	Anthocyanin, 43.2 mg	
Soybean sprout	Isoflavone, 25–36 mg	Maintaining bone health
Tomato	GABA, 12.3–20 mg	Maintaining normal blood pressure
Tomato	Lycopene, 22 mg	Decreasing LDL cholesterol levels
Enokidake mushroom	GABA, 12.3 mg	Maintaining normal blood pressure
Chili pepper	Luteolin, 5 mg	Suppressing postprandial serum glucose elevation
Spinach	Lutein, 10mg	Increasing ocular pigment contents
Kale	GABA, 12.3mg	Maintaining normal blood pressure
Kale	Lutein, 10 mg	Supporting focus adjustment functions and conditions of eyes
Sprout	Sulforaphane, 24 mg	Reducing high ALT levels
Great amberjack	EPA, 240 mg/DHA, 620 mg	Decreasing serum triglyceride levels
Yellowtail fish	EPA 300 mg/DHA, 900 mg	Decreasing serum triglyceride levels
Egg	EPA 39 mg/DHA, 352 mg	Decreasing serum triglyceride levels
Chicken breast	Imidazole dipeptide, 1 000 mg	Reducing physical fatigue and increasing the accuracy of memory
Pork thigh	Carnosine, 200 mg	Reducing physical fatigue and increasing the accuracy of memory
Pecan nuts	Oleic acid, 16.2 g	Reducing LDL cholesterol levels
Oilseed perilla	Rosmarinic acid, 50 mg	Alleviates feelings of discomfort in the eyes and/or the nose following exposure to house dust
Green tea "Benifuuki"	*O*-Methylate catechin, 34 mg	Alleviates feelings of discomfort in the eyes and/or the nose following exposure to house dust
Green tea "Sunrouge"	EGCG, 140.2 mg	Suppressing postprandial serum glucose elevation
Barley	β-Glucan, 1.055g	Suppressing postprandial serum glucose elevation
Herring roe	DHA, 265 mg; EPA, 155 mg	Decreasing serum triglyceride levels

Table 3. Freely available systematic reviews published by NARO

Agricultural products	Functional ingredients (recommended daily intake)	Function claims
Green tea	*O*-Methylated catechin (34 mg)	Alleviation of eye and nose discomfort caused by exposure to house dust
Satsuma mandarin	β-Cryptoxanthin (3 mg)	Maintaining bone health by assisting in the functioning of bone metabolism
Spinach	Lutein (10 mg)	Increased pigmentation of the retina (macula), which protects the eyes from light stimulation
Apple	Procyanidin (110 mg)	Ability to reduce body fat (visceral fat)
Vegetables, fruits, mushrooms	GABA (20 mg)	Ability to lower blood pressure in people with high blood pressure
Barley	β-glucan (1.05 g)	Ability to control the rise in postprandial blood glucose levels
Soybean	Isoflavone (23.3 mg)	Functions to help maintain bone components
Green tea	Epigallocatechin gallate (EGCG) (140.2 mg)	Ability to control the rise in postprandial blood glucose levels
Chicken and fish	Imidazole dipeptide (400 mg)	Reduction of physical fatigue
Tomato	Lycopene (27.8 mg)	Ability to lower LDL cholesterol levels
Chicken and fish	Anserine (50 mg)	Ability to lower high uric acid levels
Fish, shell	DHA (880 mg)	Ability to maintain memory
Fish, shell	DHA/EPA (860 mg)	Ability to lower triglyceride levels

cryptoxanthine (JAS0003) [(x)], lutein (JAS0008) [(xi)], and lycopene (JAS0009) [(xii)] were standardized, and analysis methods of procyanidin and ornithine are currently under investigation. In the future, when exporting high quality agricultural products with guaranteed functional ingredients to Asia and other parts of the world, it will be necessary to report the analysis methods and quality control methods of the functional ingredients to ensure consistent functional ingredients per the international JAS standards.

Revised guidelines and guidelines for subsequent checking

As mentioned above, there was a partial revision of the guidelines for the FFC system in March 2019 [(xiii)]. Among these, the following amendments were made for fresh foods, as shown in Table 4:

(1) The addition of a label stating that a portion of the recommended daily intake can be taken (e.g., This product contains A (an ingredient involved in functionality), and it has been reported that if you take X mg/day of A, it has the function B. Eating Y amount of this product will provide Z % (50 % or more) of the amount of functional ingredients per day reported to be functional.) In this case, the functional ingredients are limited to those that can be taken in general.

(2) Simplification of notification materials (30 % reduction in the number of input items), and speeding up of the confirmation of notification (speeding up the notification procedure for "re-notified products," which are changes to the extent that the identity of a published notification is not lost).

(3) Expansion of the scope of data on a product's effects on people with minor illnesses (with regard to the handling of data, including people with mild illnesses among the participants of the human clinical trials, it is now possible to use data on allergies, uric acid levels, and cognitive function as FFC notification materials, in addition to cholesterol, triglycerides, and hypertension, which are currently available as FOSHU test methods).

(4) The operation of "Borderline pharmaceuticals to non-pharmaceuticals" (food and drugs are regulated by the Food Sanitation Law and the Act on Quality, Efficacy, and Safety of Drugs and Medical Devices, or the Pharmaceutical and Medical Devices Law, respectively.) Ingredients of medicinal

Table 4. Key points of revision in the guidelines for the FFC system related to fresh food

	Revised points
1	Simplification of registered materials
2	Speeding up the verification of registrations
3	Expanding the Q&A to focus on fresh foods
4	Addition of a label that allows you to take portions based on the recommended daily intake
5	Expanding the scope of handling data on patients with minor injuries in clinical trials
6	Clarification of the approach from borderline of pharmaceuticals to that of non-pharmaceuticals
7	Expansion of the substances subject to registration (sugars and carbohydrates)

products listed as "raw materials exclusively used as pharmaceuticals," whether or not fresh food containing the ingredients themselves or the processed products of the ingredients (including traditionally fermented food and food in the form of dietary supplements) fall under the category of medicinal products, was also announced in the Q&A. This clarifies the process of confirmation by the Consumer Affairs Agency to whether or not the functional ingredients of the food to be notified are considered to be ingredients of a pharmaceutical product. If the ingredient does not fall into the category of a pharmaceutical product, it can be reported under the FFC even if it is on the above list. Examples of ingredients include deoxynodirimycin, S-adenosylmethionine, and gamma oryzanol. However, if it is unclear whether the drug falls under the category of pharmaceutical products, the question will be referred to the Ministry of Health, Labor, and Welfare.

(5) Expansion of ingredients subject to notification (mainly sugars and saccharides, excluding ingredients used as energy sources, such as glucose, fructose, galactose, sucrose, lactose, maltose, and starch).

(6) Expansion of the Q&A on fresh food.

In addition, from April 2020, the Guidelines for Ensuring Transparency of Subsequent Regulation of FFC Based on Related Laws and Regulations (Guidelines for Subsequent Checking) [(xiv)] were put into effect (Table 5). This guideline identifies cases of clearly inappropriate scientific grounds for functional labeling and advertisements that may cause legal problems. To promote sound advertising and other business activities and to ensure that consumers have the opportunity to choose products voluntarily and rationally, the objectives are to ensure the transparency of ex-post regulations (subsequent checking) based on the Act for Preventing Unjustifiable Premiums and Misleading Representations and the Health Promotion Act, to increase the predictability of operators of inappropriate labeling, and to facilitate self-inspection by operators and self-regulation by industry associations.

Table 5 shows a collection of example cases where the scientific evidence of functionality is clearly inappropriate, and of advertising and labeling that is clearly in conflict with relevant legislation. In June 2020, an industry association set up an Evidence Review committee to judge the validity of scientific evidence for gray areas that are difficult to identify even in the guidelines for subsequent checking. In the future, if the CAA rules that the validity of certain evidence is questionable, the business will have the option of (1) accepting the point and withdrawing the notification, or (2) rebutting it on its own and asking the Industrial Evidence Review Committee to evaluate it.

Increase in new functional category labeling

The number of functional categories that are not included in FOSHU is increasing, and the types and number of functional labels are also increasing. The bioeconomy strategy 2020 [(xv)] released by the Cabinet Office in June 2020 states that in order to capture the domestic and overseas market for the lifestyle-improving health care industry, it is necessary to accumulate scientific knowledge and expertise on FFC-labeled products and to provide new functional labeling, for example, indicating improved immune function.

In the immunity-related field, several products have already been accepted and placed on the market for anti-allergic effects, but those products indicated for the maintenance of immune functions have been slow to be accepted. However, thanks to the above-mentioned encouragement, five foods (three processed foods and two dietary supplements) indicated for the maintenance of immune function were registered for notification on June 19, 2020. Such products contained labels such as this: "This product contains Plasma lactic acid bacteria (*Lactobacillus lactis* strain Plasma). Plasma lactic acid bacteria act on pDCs (plasma cytoid dendritic cells) and have been reported to help maintain immune function in healthy people." It is explicitly stated that, "The functions of pDCs, including HLA-DR and CD86 expression, have been confirmed and have been shown to improve cold-related health conditions."

Table 5. Key points of the guidelines for subsequent checking

	Key points of guidelines
Examples of inadequate scientific evidence of functionality	No human intervention trials have been pre-registered
	Absence of control group that consumes the placebo diet
	Groups are not randomly assigned
	No statistically significant difference (5 % level of significance) in the primary outcome between groups
	The only significant difference in results was between pre- and post-take, not between groups
	There was a significant difference in the secondary outcome assessment, but no significant difference in the primary outcome
	Papers accepted for research review are not peer-reviewed manuscripts
Examples of advertisements and representations that are clearly in conflict with relevant laws	Disease-affected individuals were included as subjects in accepted research review articles
	Deviates from the scope of the registered function claims
	Emphasis added by quoting only part of the registration material
	Show the recommendations of doctors and experts
	Graphs and figures are cut out and shown as if the effect is more than that of the actual result
	Emphasis on ingredients that are not functionally involved ingredients that have been notified
	Labeling that is misunderstood as having been evaluated or licensed by the government

The key point of the registration is that 'immunity' was reworded from 'general malaise, chills, fever, joint pain, nasal discharge, nasal obstruction, sore throat, coughing, and physical condition or fatigue', with a focus on the activation of pDCs as the mechanism of action. In the future, the maintenance of mucosal immunity, with a focus on secreted IgA, and the maintenance of the phagocytic capacity of macrophage cells may be used as indicators of innate immunity. This is one area where the mechanism of action is expected to expand.

Conclusion

One future challenge will be to establish new methods for human intervention trials to evaluate the effects of agriculture, forestry, and fisheries products and diets that are much milder in effect than drugs in terms of health maintenance and promotion. Specifically, we need to develop ways to keep people from dropping out of long-term intervention trials of agricultural, forestry, and fishery products and diets whose effects are not clearly perceptible, as is the case with drugs, and to agree on ethically sound dietary practices, such as the restrictions on diets other than the intervention diet, as well as the issue of placebos for functional agricultural products. In addition, it is important to develop a system for sensing health problems, including states of minor physical and mental complaints, and to develop functional food products that improve these minor physical and mental complaints in individuals. Although significant differences between groups have been required in previous randomized groups comparative to human intervention trials, if the aforementioned indices are to be used, it is necessary to discuss how to make use of the differences before and after individual participation in the intervention.

Currently, nutritional components (e.g., the nutrients that cause deficiency), and functional ingredients (chemical components that do not cause deficiency) are clearly separated and labeled. However, in many countries, nutritional components and functional ingredients are treated as simply nutritional components, without distinguishing between the two. In Japan, both components should be treated in the same way as ingredients that can maintain and promote health, and it is important to redesign the FFC system to make it easier for consumers to understand by distinguishing it from the FOSHU and FNFC systems. In addition, future research on the combined effects of food combinations should be conducted to clarify the importance of diet, and to promote consumer understanding that the health functions of agricultural, forestry, and fisheries products and diets can be demonstrated through long-term, continuous consumption. For this reason, it will be increasingly important to provide systematic education from early childhood about how food supports health.

Acknowledgements The author would like to thank Enago (www.enago.jp) for the English language review.

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