

Japanese Functional Food Update Vol. 2 Foods with Function Claims notification as final product: Rectifying gut environment

In the previous issue of Functional Food Update, foods with function claims (FFC) that displayed “reducing body fat” were introduced. Presently, among products of food with function claims that have their notifications accepted by the Consumer Affairs Agency (CAA), the number of notifications of the claim “reducing body fat” is found to be the highest, followed by “rectifying gut environment”. In this issue, we will be looking into the types of food products that are notified under this claim and the evaluation items that are commonly used in related clinical trials, as well as potential challenges in terms of trial design in the future.

- Dosage forms of products notified using the claim “rectifying gut environment”

Among products that are accepted by the CAA so far, tablets and powder take up about 70% while the other 30% are in the forms that can be readily consumed (Figure1).

- Evaluation items used for functionality assessment

Outcome parameters used for evaluation of functionality can be broadly divided into 3 major types, those related to the characteristics and forms of stool (Odour, type and colour), those related to bowel movement (Degree of evacuation, amount of stool passed, bowel frequency), and the composition of intestinal microbiota (Abundance of Bifidobacterium in stool). In most clinical trials, multiple evaluation items are used (Figure 2). A detailed search into the evaluation methods for stool type used in clinical trials found out that within available methods, the commonly used Bristol Stool Scale and charts similar to the said scale are the major ones. On the other hand, various methods for evaluation of bowel frequency and amount of stool passed are used. While in some trials, participants are asked to count the total number of bowel movement in a week and to estimate the amount of stool passed by referencing to everyday objects such as egg and film case, some used the CAS-MT (Japanese version of the Constipation Assessment Scale) and asked participants questions about items such as “less frequent bowel movements”, “small stool size”, to assess

the subjective judgment of participants in relation to their bowel condition. In addition to the subjective judgment-based method, the T-RFLP (Terminal Restriction Fragment Polymorphism) is employed to assess the abundance of Bifidobacterium in stool in most of these trials.

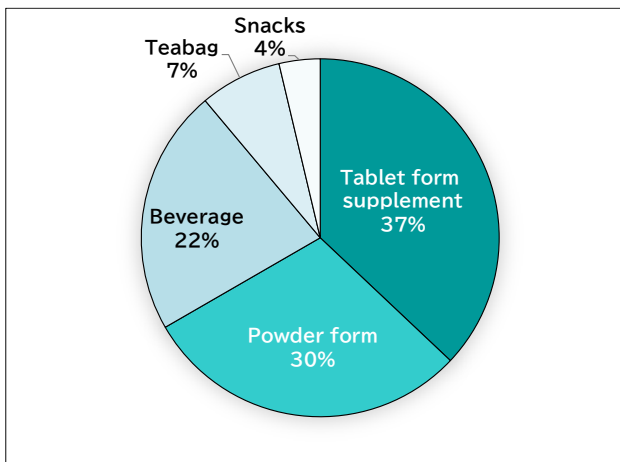


Figure 1. Number of notifications for each dosage form

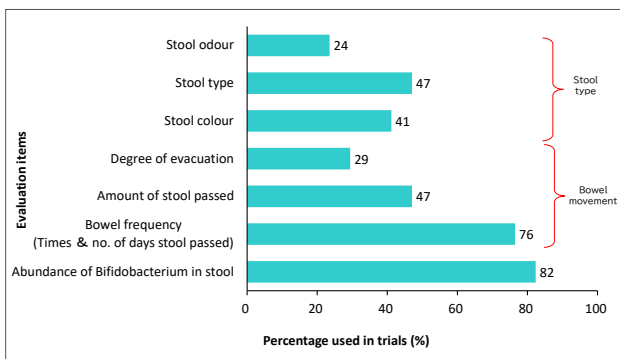


Figure 2. Relative usage percentages of various evaluation items

- ※1 Multiple evaluation items are used in combination in some clinical trials
- ※2 Evaluation items that are equal to or below 20% are excluded from the bar chart

● Issues related to the evaluation method of functionality

An investigation to the self-assessments of scientific evidence by notifiers in relation to the functionality of their notified products revealed that as many as half of the products were deemed to be “review and improvement of evaluation methods necessary” (Figure 3). This indicates that evaluation items need to be carefully selected when conducting such clinical trials.

In order to reduce the concerns and worries regarding the setting of evaluation items of our clients as much as possible, detailed review on past findings and related literature are conducted to ensure protocols that can bring about high-quality clinical trials are proposed.

Furthermore, we provide “total support” from clinical trials to post-trial related work such as notification submission and dealing with responses from the CAA. Please feel free to contact us to know more.

We will continue to provide you with information about the Japanese functional food regulation and market. Looking forward to working with you in the future.



Breakdown of review result of notifications

- Since no dietary survey or dietary restrictions were conducted on the subjects, the effects of ingestion of the test product cannot be considered to be rigorously evaluated.
- Since subjects were limited to "those with infrequent defecation", the effects of the product on all healthy individuals cannot be considered to be rigorously evaluated.
- Climatic influences cannot be ruled out because the trial period is not conducted all-year-round.
- Placebo effect on bowel movement cannot be ruled out.
- Since many evaluation items are based on subjective judgments, objective scales and appropriate questionnaires should be introduced.
- There are problems in statistical analysis, such as failure to consider multiplicity of evaluation

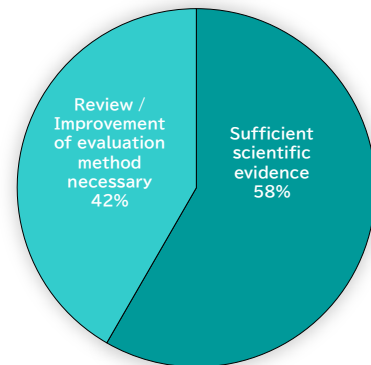


Figure 3. Review of notifier in relation to functionality

(Basic information in relation to the scientific evidence for FFC notification – Aggregation of results obtained from CAA)

Table 1. List of published clinical trials that studied final product and showed scientific evidence for "Rectifying the intestinal environment" function

FFC Notification No.	Publication	Functional Ingredient	Dosage Form	Outcomes used in functionality evaluation
B41	Sugawara T, et al (2016) ¹⁾	<i>Lactobacillus gasseri</i> CP2305	Beverage (Non-alcoholic, non-dairy beverage)	Frequency of bowel movement, stool odour, T-RFLP (Abundance of Bifidobacterium in stool), metabolites of intestinal bacteria
B218	Oda Y, et al (2015) ²⁾	Salacinol derived from Salacia	Tablet	T-RFLP (Abundance of Bifidobacterium in stool)
B232	Minamida K, et al (2015) ³⁾	<i>Bacillus coagulans</i> lilac-01	Powder	Frequency of bowel movement, degree of evacuation, stool type (Bristol Stool Scale), stool colour, amount of stool passed, stool odour
B569	Uesaki S, et al (2016) ⁴⁾	Lactoferrin	Tablet	T-RFLP (Abundance of Bifidobacterium in stool), stool type
D99				
C308	Toda T, et al (2017) ⁵⁾	<i>Lactococcus lactis</i> subsp. <i>cremoris</i> FC	Tablet	Frequency of bowel movement, amount of stool passed, stool type
D245	Fuke N, et al (2017) ⁶⁾	<i>Lactobacillus brevis</i> KB290, β-carotene	Tablet	Abdominal pain, amount of stool passed, serum concentration of cytokines
D303	Sugiyama K, et al. (2017) ⁷⁾	Cacao Lignin	Powder	Stool odour, stool frequency, stool type (Bristol Stool Scale)
D460	Najima M, et al (2017) ⁸⁾	Inulin, chlorogenic acid	Teabag	Amount of stool passed
D461				
D653	Iwasaki S. et al (2017) ⁹⁾	Salacinol derived from Salacia	Beverage (Milk product: Lactobacillus beverage)	T-RFLP (Abundance of Bifidobacterium in stool), CAS-MT (Abdominal discomfort)
E773				
E860				
F524				
F582				
D674				
D675	Sakai R. et al (2017) ¹¹⁾	Genkwanin 5-O-β-primeveroside, mangiferin	Tablet	Stool frequency, degree of exacuation
E292				
E4	Hoshino T. et al (2018) ¹²⁾	Resistant dextrin (As dietary fibre), galactooligosaccharide	Snack (Jelly)	T-RFLP (Abundance of Bifidobacterium in stool), CAS-MT (Stool frequency, amount of stool passed, abdominal discomfort, rectal pain with bowel movement)
E58	Najima M, et al (2018) ¹³⁾	Enterococcus faecalis (EC-BabyM), indigestible dextrin (dietary fiber)	Powder	Stool frequency, T-RFLP (Abundance of Bifidobacterium in stool)
E555	Nishida K, et al (2017) ¹⁴⁾	<i>Lactobacillus gasseri</i> CP2305	Tablet	Abundance of Bifidobacterium in stool, stool colour
E745				
F263				
E797	Kobayashi M. et al (2019) ¹⁵⁾	Indigestible dextrin (Dietary Fibre), <i>Bacillus coagulans</i> SANK70258, fructooligosaccharide	Powder	Stool frequency, RT-PCR (<i>Bifidobacterium</i> count in stool)
E823				
F772	Matsui N. et al (2011) ¹⁶⁾	Young Barley Leaf powder (Dietary fibre)	Powder	Stool frequency, amount of stool passed, degree of exacuation
F1017	Nishihira J, et al (2019) ¹⁷⁾	Holocellulose derived from Kumaizasa powder	Powder	Stool frequency, stool odour, Visual Analogue Scale

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