Japan's Approval Process for Food Additives
“Additives" mean substances that are used by being added, mixed or infiltrated into food or by other methods.

- in the process of producing food

or

- for the purpose of processing or preserving food

(Article 4 of the Food Sanitation Act)
Definition and Scope of Food Additives in Japan

Food additives include:
- Enzymes
- Nutrients
- Flavorings
- Processing aids (e.g. disinfectants, extraction solvents)
- Post-harvest fungicides
- Substances that are categorized as additives in the EU, such as preservatives and food colors

Food additives are treated equally, regardless of whether they are derived from natural sources (e.g., animals and plants) or are chemically synthesized.
Article 10 of the Food Sanitation Act
Additives (excluding natural flavoring agents and ordinary foods used as food additives), additive preparations and foods containing additives shall not be sold; nor be produced, imported, processed, used, stored or displayed for the purpose of marketing, except for cases where the Minister of Health, Labour and Welfare has specified there is no risk to human health by hearing the opinions of the Pharmaceutical Affairs and Food Sanitation Council.

Guidelines for the Designation of Food Additives and Revision of Standards for Use of Food Additives
Food additives shall not pose a risk to human health and their use must provide benefits to consumers.

Food Additives are not permitted for use unless proven safe and effective.
<table>
<thead>
<tr>
<th>Category</th>
<th>Definition</th>
<th>No. of substances(^1)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Designated additives</td>
<td>Substances that have been designated by the Minister based on Article 10 of the FSA</td>
<td>454(^2)</td>
<td></td>
</tr>
<tr>
<td>Existing Additives</td>
<td>Additives that were permitted for use at the time of the 1995 revision of the FSA(^<em>), as exception, without having gone through the designation process, for the reason that they had been widely used in Japan and had a long history of human consumption. They are specified on the List of Existing Additives. (^</em>) The 1995 amendment expanded the designation process to natural additives.</td>
<td>365(^3)</td>
<td>Existing Additives will be delisted if problems with their safety are discovered or they are no longer in use.</td>
</tr>
<tr>
<td>Natural flavoring agents</td>
<td>Substances that are derived from natural sources, such as animals and plants, and used for flavoring purposes</td>
<td>Ca.600(^4)</td>
<td>Exempt from designation as additives</td>
</tr>
<tr>
<td>Ordinary foods used as food additives</td>
<td>Substances that are generally used for eating or drinking as food and also used as food additives</td>
<td>Ca.100(^5)</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) as of 7 December 2017  
\(^2\) [http://www.ffcr.or.jp/zaidan/FFCRHOME.nsf/pages/list-desin.add-x (English)](http://www.ffcr.or.jp/zaidan/FFCRHOME.nsf/pages/list-desin.add-x (English))  
\(^3\) [http://www.ffcr.or.jp/zaidan/FFCRHOME.nsf/pages/list-exst.add (English)](http://www.ffcr.or.jp/zaidan/FFCRHOME.nsf/pages/list-exst.add (English))  
\(^5\) [http://www.ffcr.or.jp/zaidan/FFCRHOME.nsf/pages/list-general.provd.add (English)](http://www.ffcr.or.jp/zaidan/FFCRHOME.nsf/pages/list-general.provd.add (English))
Flavoring agents are permitted for use only when they are designated by the Minister for flavoring purposes. Currently, **about 130 substances and 18 chemical categories are designated**. Substances falling under the designated categories can be used as flavoring agents.

1. Isothiocyanates* \( R_1 \)-NCS
2. Indoles and Its Derivatives
3. Ethers \( R_1 \)-O-\( R_2 \)
4. Esters \( R_1 \)-COOR\(_2\)
5. Ketones \( R_1 \)-COOH
6. Fatty Acids \( R_1 \)-COOH
7. Aliphatic Higher Alcohols
8. Aliphatic Higher Aldehydes*
9. Aliphatic Higher Hydrocarbons*
10. Thioethers* \( R_1 \)-S-\( R_2 \), \( R_1 \)-SSS-\( R_2 \)
11. Thiols (Thioalcohols)* \( R_1 \)-SH
12. Terpene Hydrocarbons
13. Phenol Ethers*
14. Phenols*
15. Furfurals and Its Derivatives*
16. Aromatic Alcohols
17. Aromatic Aldehydes*
18. Lactones*

Note: Substances marked with asterisk exclude those generally recognized as highly toxic. “Higher” means C6 or higher.
Specifications and Standards of Food Additives

Food Sanitation Act

**Article 10**
Prohibition of sale of Unapproved food additives

**Article 11**
Standards and specifications for foods and food additives

Specifications and Standards for Foods, Food Additives, etc.
(Ministry of Health, Labour and Welfare, Notification)

I. Foods

II. Food Additives
(specifications and standards are established)
Example of Specifications and Standards

Benzoic Acid (preservative)

**Specifications**

<table>
<thead>
<tr>
<th>Specification</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Content</td>
<td>Not less than 99.5%</td>
</tr>
<tr>
<td>Description</td>
<td>White laminar or needle crystals Odorless or slight odor of benzaldehyde</td>
</tr>
<tr>
<td>Identification</td>
<td>A solution of 1 g of the sample in 20 mL of a 1 in 25 solution of sodium hydroxide responds to test (2) for Benzoate</td>
</tr>
<tr>
<td>Melting point</td>
<td>121–123°C</td>
</tr>
<tr>
<td>Purity</td>
<td>(1) Lead Not more than 2 µg/g as Pb (2) Arsenic Not more than 3 µg/g as As</td>
</tr>
</tbody>
</table>

**Standards**

Caviar ($\leq 2.5$ g/kg), Margarine ($\leq 1.0$ g/kg), Nonalcoholic beverages ($\leq 0.60$ g/kg), Soy sauce ($\leq 0.60$ g/kg) and Syrup ($\leq 0.60$ g/kg)

When the additive is used in margarine with Sorbic Acid, Calcium Sorbate or Potassium Sorbate, or a preparation containing one of these additives: The sum of the amount as benzoic acid and the amount as sorbic acid $\leq 1.0$ g/kg
Approval Procedures for Food Additives

The Food Safety Commission of Japan (FSC) assesses the risk to human health of food additives. The Ministry of Health, Labour and Welfare (MHLW) designates food additives based on the risk assessment by the FSC.

**FSC**
- **Risk Assessment**
  - Toxicity Evaluation
    - Chronic toxicity
    - Carcinogenicity
    - Reproductive and developmental toxicity, etc.
  - ADI (draft)
  - Public comments
  - Set the ADI
- **Hearing**
- **Notice**
  - Notice Recommendation

**MHLW**
- **Receive an application**
- **Examine documents**
- **Request assessment**
- **Confirm the ADI**
- **Review standards**
- **Notify the WTO, public comments**
- **Ministerial Ordinance, Notification (draft)**
- **Revise Ordinance & Notification**
- **Consult**
- **Report**

**Applicant**

**Consumer Affairs Agency (CAA)**
- **Response**

**Pharmaceutical Affairs and Food Sanitation Council (Food Safety Council Committees)**
The standard processing period for the designation process of food additives
• One year for the risk assessment by the FSC
  - Time from when the MHLW requests the FSC to carry out the risk assessment to when the MHLW is notified of the assessment results by the FSC
• One year for approval procedure by the MHLW
  - Time from when the MHLW is notified of the risk assessment results to when the target additive is designated

The standard processing period does not include:
Time needed for the applicant to prepare and submit additional documents in response to the request by the FSC or the MHLW

(FSC decision, 16 July 2009)
(MHLW Notice, 10 June 2016)
Guidelines for the Designation of Food Additives and Revision of Standards for Use of Food Additives

(MHLW Notice No. 29, 22 March 1996)

Purpose:
• The guidelines are designed to outline the procedures required to apply for the designation of food additives, pursuant to Article 10 of the Food Sanitation Act, and for the establishment of use standards for food additives, pursuant to Article 11.
• The guidelines provide details of the documents to be submitted for application, such as information on safety data and recommended methods for safety studies.

Documents

- Application form (Japanese only)
- Accompanying documents
- Overview Documents
- Reference documents (Japanese or English)
I. Information on the food additive to be assessed
1. Name and uses
2. Origin or details of development
3. Usage in foreign countries
4. Assessments by national and international organizations
5. Physicochemical properties
6. Use standards (draft)
7. Other

II. Findings regarding effectiveness
1. Effectiveness as food additive and comparison with other additives with the same use
2. Stability in food
3. Effects on nutritional components in food

III. Findings regarding safety
1. Toxicokinetics studies (ADME)
2. Toxicological studies
3. Findings in humans
4. Estimation of daily intake

IV. References
Flow of the Risk Assessment

1. Request for risk assessment
2. Hear the background and details of the request from MHLW
3. Deliberations on safety
4. Prepare draft risk assessment reports
5. Invite comments from the public (generally for 30 days)
6. Consider public opinion/information
7. Finalize risk assessment reports
8. Notification of the risk assessment results

Risk managers (MHLW)

Food Safety Commission
Guidelines for the Risk Assessment

- Risk assessments of food additives are performed in accordance with “Guideline for Assessment of the Effect of Food on Human Health Regarding Food Additives” (FSC, May 2010, rev. July 2017).

- This guideline is available on the FSC’s website. 
# Information Required for Risk Assessments

<table>
<thead>
<tr>
<th>Items</th>
<th>Designation</th>
<th>Revision of standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information on the additive subject to assessment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Name and usage</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>2. Origin or process of discovery</td>
<td>Required</td>
<td>*</td>
</tr>
<tr>
<td>3. Usage in other countries</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>4. Assessments by international organizations and other organizations</td>
<td>Required</td>
<td>*</td>
</tr>
<tr>
<td>5. Physicochemical properties</td>
<td>Required</td>
<td>*</td>
</tr>
<tr>
<td>6. Suggestions for usage standards</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>7. Others (Information useful for assessments of the effect of food on health)</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

Findings regarding safety

1. Studies on toxicokinetics (ADME)                                   | Required    | *                    |
2. Toxicity                                                          |             |                      |
   (1) Subchronic toxicity studies and chronic toxicity studies        | Required    | *                    |
   (2) Carcinogenicity studies                                         | Required    | *                    |
   (3) Toxicity/Carcinogenicity combination studies with one-year repeated-dose administration | Required    | *                    |
   (4) Reproductive toxicity studies                                  | Required    | *                    |
   (5) Prenatal developmental toxicity studies                        | Required    | *                    |
   (6) Genotoxicity studies                                           | Required    | *                    |
   (7) Allergenic potential studies                                   | Required    | *                    |
   (8) General pharmacological studies                                | Required    | *                    |
   (9) Other studies                                                  | *           | *                    |
3. Findings in humans                                                | Required    | *                    |
4. Estimation of daily intake etc.                                    | Required    | Required             |

* : submitted as necessary
Information Required for Risk Assessments

- When applicants apply for extension of use of food additives for which the FSC has already conducted a risk assessment, the materials required for “Revision of standard” should be submitted.

- When applicants apply for extension of use of food additives for which the FSC has not conducted a risk assessment (e.g. in cases where those additives are “Existing Additives” or they were designated before the FSC was founded), the materials required for designation should be submitted, in principle.
The latest guideline on risk assessments of food enzymes was issued in July 2017.

Information required for risk assessments

- Information on the food enzyme to be assessed
  - Name and uses, origin or backgrounds of discovery, usage in other countries, assessments by international and other organizations, physicochemical properties, draft conditions of use, other useful information

- Findings regarding safety
  - Safety of the organism of origin
  - Degradability of the food enzyme in the digestive tract
  - Toxicity
    - 90-day repeated-dose toxicity study
    - Genotoxicity study
    - Allergenic potential study

- Estimation of daily intake
The latest guideline on risk assessments of nutrients was issued in July 2017.

Information required for risk assessments

- Information on the nutrient to be assessed
  - Name and uses, origin or backgrounds of discovery, usage in other countries, assessments by international and other organizations, physicochemical properties, draft conditions of use, other useful information

- Findings regarding safety
  - Toxicokinetics (ADME)
  - Findings in humans
    - Table of evidence characteristics for effects observed in humans
    - Case reports
    - Meta-analysis
  - Toxicity

- Estimation of daily intake
Information Required for Risk Assessments

Flavoring agents

- Guidelines for the Designation of Flavoring Agents (MHLW, May 2016)
  - Documents to be submitted for the application for designation of flavoring agents
    - Overview documents
    - Documents on the origin or details of development and use status in other countries
    - Documents on the physicochemical properties and specifications
    - Documents on effectiveness
    - Documents on safety

- Guidelines for the Assessment of Flavoring Substances in Foods on Health (FSC, May 2016)
  - Information required for risk assessments
    - Information on the flavoring substance to be assessed
    - Genotoxicity
      - Genotoxicity studies and others
    - General toxicity
      - The structural classification of the flavoring substance, metabolic studies, and others
    - Estimation of daily intake (MSDI method)
To facilitate the designation process:

- The consultation center (FADCC) has been set up in the National Institute of Health Sciences, MHLW to advise applicants on how to prepare application documents. [Link](http://www.nihs.go.jp/dfa/fadcc/e_fadcc/fadcc_ehome.html)

- A practical guide for applicants has been issued by the MHLW. “The Procedure for Preparing Application Documents for Designation of Food Additives and Revision of Use Standards for Food Additives” (MHLW, 9 September 2014)
How to Prepare Application Documents

The Procedure for Preparing Application Documents for Designation of Food Additives and Revision of Use Standards for Food Additives
(MHLW Notice, 9 September 2014)

■ Purpose
  • Deepen applicants’ understanding of the designation procedure for food additives
  • Help applicants efficiently prepare application documents

■ Outline
  • This guide explains how to write the application documents, based on the guidelines published in MHLW Notice of 22 March 1996.
  • It contains:
    ➢ explanations
    ➢ points to which attention should be paid
    ➢ how to collect relevant information
    ➢ examples of description for each item.

An English version is available at
More Information on Food Additives in Japan

**Ministry of Health, Labour and Welfare, Japan**
- Food Additives Homepage (in English)
  - Guidelines for the Designation of Food Additives and Revision of Standards for Use of Food Additives
  - Guidelines for the Designation of Flavoring Agents
  - The Procedure for Preparing Application Documents for Designation of Food Additives and Revision of Use Standards for Food Additives
  - Data of average intake of individual food

**Food Safety Commission of Japan**
- Top page (in English)
- Risk Assessment (in English)
  - Guideline for Assessment of the Effect of Food on Human Health Regarding Food Additives
  - Guidelines for the Assessment of Flavoring Substances in Foods on Health
- The latest guidelines (in Japanese)
  https://www.fsc.go.jp/senmon/tenkabutu/
  - Food additives, including processing aids (July 2017)
  - Food enzymes (July 2017)
  https://www.fsc.go.jp/senmon/sonota/#a1
  - Nutrients (July 2017)