

## **Annex 5.**

### The guidelines for designation of food additives, and for revision of standards for use of food additives (Excerpt)

#### I Purpose

These guidelines are designed to provide the procedures required to apply for designation of substance intended to be used as food additives pursuant to Article 6 of the Food Sanitation Law and to apply for establishment of use standards for food additives pursuant to Article 7, Paragraph 1 of the same law. Also, these guidelines provide the scope of accompanying documentation for these applications and the recommended methods for safety studies that are required to prepare the documentation.

#### II Principles for designation and revision of standards for use of food additives

Food additives must pose no hazards to human health and be effective. Also, the use of them must benefit consumers. In designating food additives and revising use standards, the points given below must be scientifically confirmed. Scientific evaluations will be conducted by the Pharmaceutical Affairs and Food Sanitation Council from the view of the public health. In these evaluations, standards of the Joint FAO/WHO Codex Alimentarius Commission and conditions of Japanese food intake will be considered.

##### 1. Safety

The safety of the targeted food additive should be proven or confirmed in the intended methods of use.

##### 2. Effectiveness

It should be proven or confirmed that the use of the food additive comes under one or more of the purposes set out in (1) to (4) below. However, where the manufacturing or processing method for a target food can be improved or modified at comparatively low cost, and the improved or modified method does not require the food additive for the manufacture or processing of the food, the use of the food additive is not justified.

(1) To preserve the nutritional quality of the food.

An intentional reduction in the nutritional quality of a food would be justified in the circumstances dealt with in section (2) below and also in other circumstances where the food does not constitute a significant item in a normal diet.

(2) To provide necessary ingredients or constituents for food manufactured for groups of consumers having special dietary need, provided that the food additive is not intended to provide medical effects, such as prevention or treatments of certain diseases.

(3) To enhance the keeping quality or stability of a food or to improve its organoleptic properties, provided that this does not so change the nature, substance, or quality of the food as to deceive the consumer.

(4) To provide aids in the manufacture, processing, preparation, treatment, packing, transport, or storage of food, provided that the food additive is not used to disguise the effects of the use of faulty raw materials or of undesirable (including unhygienic) practices or techniques during the course of any of these activities.

### III Procedures for designation and revision of standards for use of food additives

#### 1. Application

Those who wish to apply for designation of a food additive or to apply for revision of standards for use of an food additive may submit an application to the Minister of Health, Labour, and Welfare. The application should be accompanied by any required documentation on draft specifications and use standards, and the safety of the food additive.

#### 2. Draft specifications and standards for use

(1) An application for designation of a food additive should be basically accompanied by draft specifications of the food additive. Draft standards are required only when

target foods, in which the food additive is used, the amount of its use, and the way of using are restricted.

(2) An application for revision of standards for use for a food additive should be accompanied by a list in tabular form contrasting the existing standards and the proposed standards.

### 3. Process of examination of application

Documentation submitted by an applicant will first be examined by the secretariat office. When the Minister determines it appropriate to hear opinions from the Pharmaceutical Affairs and Food Sanitation Council, then the Ministry of Health, Labour, and Welfare will start the processing required to consult the Council about the application.

The Council may ask for additional documents from the applicant if necessary. When the Council determines the designation or revision to be appropriate after due discussion, it will make an affirmative report to the Minister of Health, Labour, and Welfare. In response to the report from the Council, the Ministry of Health, Labour, and Welfare will follow appropriate formalities, including the revision of the Enforcement Regulations of the Food Sanitation Law. (See the attached diagram)

### 4. Processing period

The standard period of time required for processing, from the receipt of the application by the Ministry of Health, Labour, and Welfare to the designation or revision of standards for use, is one year. However, this period does not include any time required for completion of incomplete applications or documents submitted, or any time needed for replies to inquiries by the Council.

## IV. Documentation required for designation of food additives and revision of standards for use of food additives

### 1. Scope of accompanying documentation

(1) Applications for designation of a food additive and for revision of use standards for a food additive, as a rule, require the documentation given in the Table. However, some

documents may be exempted from submission, provided that adequate reasons for the exemption are stated.

(2) The applicant should submit any data that would raise doubts about the quality, safety, or effectiveness of the food additive, without regard to the reliability of the submitted documentation.

## 2. General considerations for preparation of documentation

(1) In preparing the required documentation for application, applicants should assume full responsibility for the reliability of the information.

(2) Basically, all documentation should be submitted in Japanese. However, the documents other than the summary (see Table 1) may be submitted in English.

(3) Studies necessary to prepare the required documentation should be conducted in laboratories that have adequate facilities, equipment, and personnel to ensure the reliability of test data, and that are recognized as adequately managed.

## 3. Specific considerations for documentation required to apply for designation of food additives

### (1) Summary of documentation

① The summary should concisely describe the documentation categories.

② If any of the documents listed in Table is exempted from submission, the reasons for that exemption should be stated.

### (2) Documentation on origin or details of development and overseas conditions on use

#### ① Origin or details of development

The history of the food additive should include a chronology of development and use. Its use in other countries should be described.

#### ② Condition on use in foreign countries

Overseas conditions (including approval status of the food additive, target foods in which the food additive is used, standards for use, and specifications) should be described. Also, safety evaluation, standards for use, and specifications for the same additive of international organizations should be described.

(3) Documentation on physicochemical characteristics and specifications

The documentation should be prepared based on results of appropriate tests conducted in accordance with the sections entitled “General Notice” and “General Tests” in the official compilation of food additives (*Japan’s Specifications and Standards for Food Additives*, former *The Japanese Standards for Food Additives*).

① Name

The generic name and chemical name (International Union of Pure and Applied Chemistry Name) should be given.

② Structural formula or rational formula

This formula should be described by referring to the description of that of a substance with a similar structure appearing in *The Japanese Standards for Food Additives*.

③ Molecular formula and formula weight

These should be described based on the section entitled “General Notice” in *Japan’s Specifications and Standards for Food*.

④ Assay

Assay requirements for the food additive should be established to ensure constant quality in safety and effectiveness based on the manufacturing process, assay error, and stability.

⑤ Methods of manufacturing

Methods of manufacturing should be clearly stated because types and amounts of impurities produced or intermixed during the manufacturing process vary with the methods for the food additive.

⑥ Description

Information necessary to identify or handle the food additive should be stated. Usually, the information includes taste, odor, color, and form.

⑦ Identification tests

Identification tests are required to identify whether the substance is the target food additive, based on its characteristics. Therefore, the tests should be specific to characteristics based on the chemical structure of the food additive.

⑧ Specific properties

Specific properties are expressed as values measured using physical or chemical means. They include absorbance, optical rotation, pH, and melting point. Parameters necessary for quality assurance of the food additive should be described.

⑨ Purity tests

Purity tests are required to determine levels of impurities in the food additive, and specify the purity of the food additive as well as assays.

⑩ Loss on drying, loss on ignition, or water content

A test for “loss on drying” is usually required to measure substances that is present in the food additive and can be lost by drying. The substances include free water, all or part of the crystalline water, and volatile substances. A test for “loss on ignition” is usually required on an inorganic substance that can lose a part of its components or admixed substances by igniting. Water determination is usually required to determine the water content in the food additive.

⑪ Residues on ignition

This test is generally required to measure the total amount of inorganic impurities present in an organic compound. In some cases, this test may be conducted to measure the amount of inorganic substances present in an organic compound as its components or the amount of impurities present in an inorganic compound that can volatilize by heating.

⑫ Method of assay

An assay method is intended to determine the content of an effective component of the food additive using physical, chemical, or biological means.

When a relative analytical method is established, specifications for the reference standard used in the analysis should be established.

⑬ Stability of food additives

The stability of the food additive including breakdown products should be evaluated. Also, the stability of decomposition products should be evaluated.

⑭ Analytical methods for food additives in food

Basically, analytical methods should be established for foods in which the food additive is likely to be used at high possibility. They should be methods to identify the addition of the food additive quantitatively and qualitatively by chemically analyzing target foods.

If other additives with similar purposes are used together with the food additive, the target additive should be separated from the additives used with and analyzed.

⑮ Principles to establish draft specifications

a) Specifications should be required to secure a constant quality concerning safety and effectiveness.

b) A list contrasting the proposed specifications and international and other major countries' specifications should be attached.

(4) Documentation on effectiveness

① Studies concerning effectiveness should be conducted to establish that the food additive has expected effects, according to its purposes.

② Comparisons in effects with a widely used food additive, which has already been approved for the same use, are desirable.

③ Studies on the stability of the food additive in foods should be conducted. For unstable food additives, breakdown products should be examined on kinds and extent.

④ Effects of the food additive on main nutrients in foods should be examined.

(5) Documentation on safety

① Documentation on toxicity

a) In order to ensure the reliability of animal toxicity study data, toxicity studies should be conducted in accordance with appropriate good laboratory practice (GLP), such as standards for the conduct of safety studies on drugs.

b) Generally used methods for each toxicity study are given in Chapter V of the Guidelines to help with adequate evaluation concerning the safety of food additives.

It is not reasonable to apply uniform methods to all food additives. New methods may be developed, keeping pace with the advance in scientific technology. If obtained findings can enable scientific safety evaluation of the food additive, examiners may not necessarily adhere to the methods specified in Chapter V. Studies complying with OECD (the Organization for Economic Cooperation and Development) guidelines or USFDA (the US Food and Drug Administration) guidelines are basically acceptable.

② Documentation on metabolism and pharmacokinetic study

a) A metabolism and pharmacokinetic study is usually required to estimate systems of absorption, distribution, metabolism, and excretion of the food additive in the living body when that additive is consumed by humans. The documentation should include not only animal test findings but discussions concerning extrapolation to humans of metabolism and pharmacokinetics and possible harmful effects.

b) General methods of metabolism and pharmacokinetic study are described in Chapter V. The conduct of this study should follow the basic concept given in ① b) in this chapter.

③ Documentation on daily intake of the food additive

a) The daily intake of the food additive is estimated by using data on the daily intake of target foods and the amount of the food additive used in each food. In determining the daily intake of the target foods in Japan, data on the food intake

obtained based on the National Nutrition Survey or other related surveys are useful.

b) Safety evaluation should be performed by comparing the daily intake of the food additive with the acceptable daily intake determined by toxicity studies. When the food additive is consumed with other similar additives, its safety should also be evaluated.

Attention should, if necessary, be given to overintake of the food additive and effect on the balance of electrolytes in the living body, in the light of conditions of Japanese food intake.

(6) Documentation on draft standards for use

① When the applicant determines that standards for use of the food additive are necessary to restrict the target foods and the amount of use, as a result of comprehensive evaluation of the safety and effectiveness of the food additive, he or she should clarify the evidence supporting the necessity of standards for use, based on the documents given in (2) through (5) above. Standards for use should be established, according to those already established for other food additives.

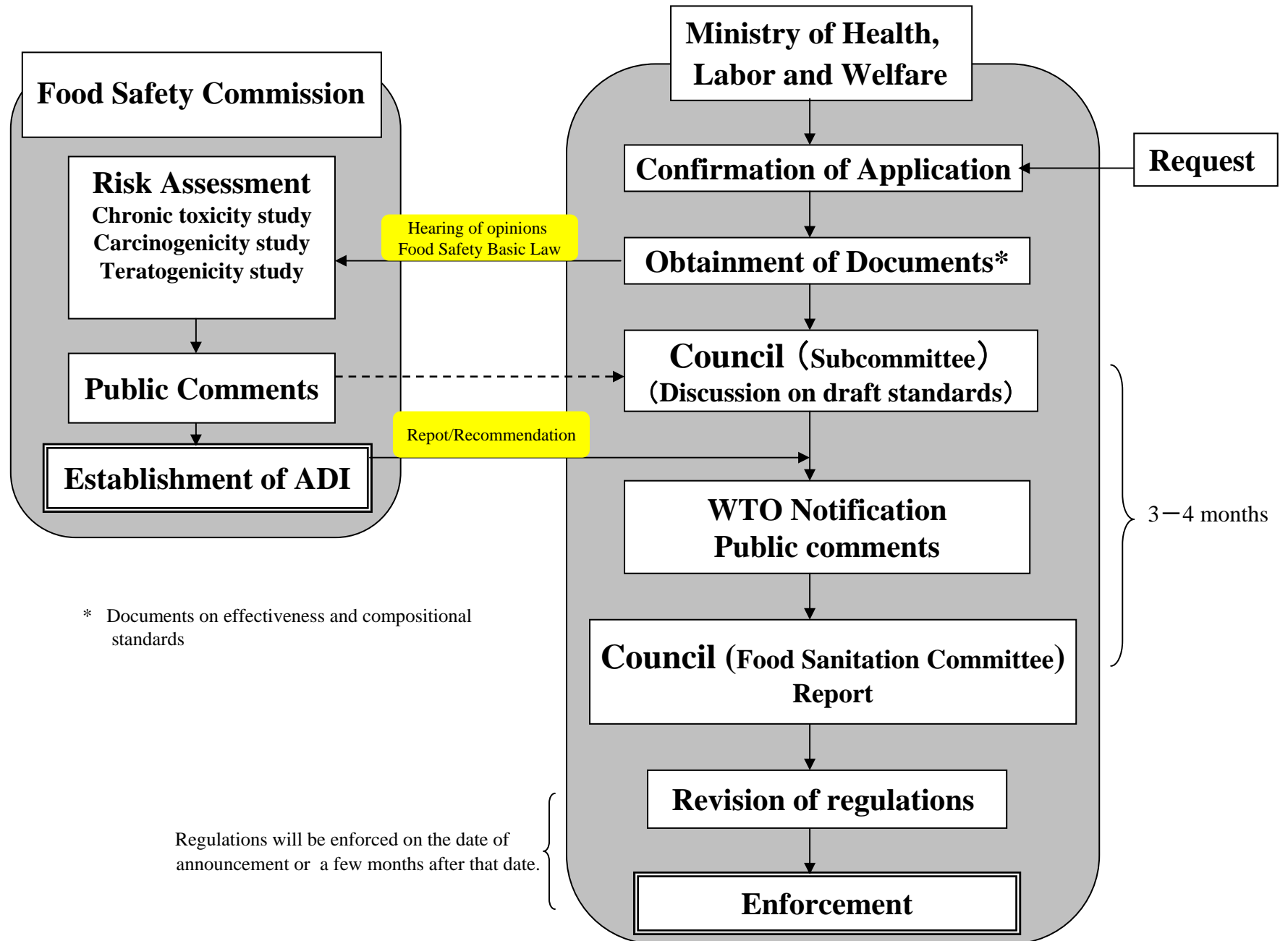
② When the applicant determines that standards for use of the food additive are not necessary, he or she should clarify the evidence supporting that determination, based on the documents given in (2) through (5).

4. Specific considerations for documentation required to apply for revision of standards for use

The applicant should follow the specific considerations given in section 3, Chapter IV. The documentation should include evidence supporting the necessity of the revision of standard(s) for use of the food additive, including the addition of target foods and the change of amount of use.

# Process of the Designation of Food Additives

Diagram



Table

**Documentation required to apply for designation of food additives  
and for revision of their standards for use**

Document Category	Approval	Revision
1. Summary	○	○
2. Chronology on origin or development and overseas use conditions		
(1) Details of origin or development	○	△
(2) Overseas use conditions	○	○
3. Physiochemical characteristics and specifications		
(1) Name	○	△
(2) Structural formula and rational formula	○	△
(3) Molecule formula and formula weight	○	△
(4) Assay	○	△
(5) Methods of manufacturing	○	△
(6) Description	○	△
(7) Identification tests	○	△
(8) Specific properties	○	△
(9) Purity tests	○	△
(10) Loss on drying, loss on ignition, or water	○	△
(11) Residues on ignition	○	△
(12) Method of assay	○	△
(13) Stability	○	△
(14) Analytical method for the food additives in foods	○	△
(15) Principles to establish proposed specifications	○	△
4. Effectiveness		
(1) Effectiveness and comparison in effect with other similar food additives	○	○
(2) Stability in foods	○	△
(3) Effects on nutrients of foods	○	△
5. Safety evaluation		
(1) Toxicity studies		
1) 28-day toxicity study	○	△
2) 90-day toxicity study	○	△
3) One-year toxicity study	○	△
4) Reproduction study	○	△
5) Teratogenicity study	○	△
6) Carcinogenicity study	○	△
7) Combined chronic toxicity/carcinogenicity study	○	△
8) Antigenicity study	○	△
9) Mutagenicity study	○	△
10) General pharmacological study	○	△
(2) Metabolism and pharmacokinetic studies	○	△
(3) Daily intake of food additives	○	○
6. Proposed standards for use	○	○

## Note:

Documents marked with the symbol, "○," are basically required.

Documents marked with the symbol, "△," should be submitted, only when considered as necessary: e.g., where new information is obtained.