

**The Nineteenth Seminar
for
Visiting Food Hygiene Experts**

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**Policy Planning and Communication Division
Standards and Evaluation Division
Inspection and Safety Division**

**Department of Food Safety
Pharmaceutical and Food Safety Bureau
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Part II

Establishment of Specifications and Standards

Based on the Food Sanitation Law

Part II Establishment of Specifications and Standards Based on the Food Sanitation Law

Introduction

The Food Sanitation Law establishes a wide variety of standards not only for foods themselves but also for food related items. These standards include food labeling standards and standards for the safety assessment of foods and food additives produced by recombinant DNA techniques. This text mainly describes the establishment of standards and specifications for food, pesticides, veterinary drugs, and food containers/packages.

1. Food

(1) Historical background

<In general>

All foods distributed in the domestic market are subject to the law (enacted in 1947). They are regulated by compositional specifications, and standards for manufacturing, processing/preparation, and storage that have been established based on the law.

The Ministry of Health, Labour and Welfare (before 2001 the Ministry of Health and Welfare) establishes specifications and standards for foods whose quality should be assured at certain levels and for perishable foods whose safety cannot be ensured without specifications and standards. For example, these foods include milk products, meat products, fish paste products, oysters for raw consumption, and frozen fish/shellfish for raw consumption. The MHLW established specifications and standards for milk and milk products in 1950 (Ministerial Ordinance concerning Compositional standards for milk, milk products, and similar products; former Ordinance), for meat products in 1954, for frozen oysters for raw consumption and fish paste products in 1962, and fish/shellfish for raw consumption in 1971. Thereafter, new types of foods started to be distributed as technology advanced. In 1977, the MHLW established specifications and standards for foods that are packed into containers/packages and pasteurized under pressure. Since then, the MHLW has revised the specifications and standards as needed. The following are specifications and standards established or revised after 1977:

1982 Unheated meat products

The new food category, unheated meat products, was established. Specifications and standards were newly established for this category, targeted at raw hum and similar products.

- 1986 Mineral water
Specifications and standards were made into the present form by adding new ones.
- 1993 Heated meat products
Specifications and standards were established for heated meat products.
- 1998 Chicken egg and liquid egg
Specifications and standards were established as preventive action against food poisoning caused by *salmonella*.
- 2001 Fish and shellfish consumer raw
Specifications and standards were established as preventive action against food poisoning caused by *Vibrio parahaemolyticus*
- 2002 Specifications and standards were established for skimmed milk powder as the preventive measure for food poisoning caused by *Staphylococcus aureus*
- 2006 Agricultural chemical residues
Based on the 2003 amendment of the Food Sanitation Law, a positive list system for agricultural chemicals was implemented.

<Milk and milk products>

Separately from other foods, milk and milk products are regulated by the “Ministerial Ordinance concerning Compositional Standards Etc. for Milk and Milk Products,” (Promulgated in 1951, Ministry of Health and Welfare Announcement No. 52), based on the law. The Ministerial Ordinance targets milk and milk products that are considered to be consumed in large amount by infants, young children, and sick and invalid people. Considering the special nature of those products, then Ministry of Health and Welfare decided that it is necessary to manage the hygiene of products to improve public health.

Ministerial Ordinance concerning Compositional Standards Etc. for Milk and Milk Products

In 1951, the Ministerial Ordinance Concerning Compositional Standards Etc. for Milk and Milk Products was established under the law and the former Ordinance was abolished. The new Ordinance targets milk and milk products, which are needed especially for infants, young children, and sick and invalid people.

In 1959, all products made mainly of milk and milk products were placed

under the jurisdiction of the Ministerial Ordinance, and the Ordinance was changed into its present form. The milk products include butter, cheese, cream, and fermented milk.

The Ordinance covers not only specifications for individual products and testing methods, but also specifications for containers and packages of milk and milk products. The Ordinance has been amended several times. The recent amendments were made in 2002 and 2003. See Section (3) “Revision of specifications and standards for milk and milk products.”

(2) Specifications and standards for fresh fish and shellfish

<Preventive measures for foodborne infections caused by *Vibrio parahaemolyticus*>

In June 2001, Japan newly established specifications and standards for seafood, mainly fish and shellfish for raw consumption. This activity was based on social background and dietary preference. Food poisoning incidents caused by *Vibrio parahaemolyticus* had been increasing since 1996. Japanese people like eating seafood raw and its consumption is very large. Under such circumstances, the MHLW initiated the establishment of specifications and standards from the viewpoint of public health, taking the lead from other countries.

Standards and requirements newly established for seafood

The following were newly established: preparation standards for all seafood products for raw consumption; compositional specifications and processing, storage and labeling standards for boiled crabs and fish fillets and shucked shellfish for raw consumption. The following were added to the existing standards: compositional specifications and processing standards for boiled octopus, raw oysters, and frozen fish and shellfish for raw consumption. See the separate document, *Specifications and Standards for Foods, Food Additives, etc. under the Food Sanitation Law (Abstracts), published by the Japan External Trade Organization (JETRO)*.

In addition, the MHLW issued recommendations about storage temperature and food handling to seafood-related businesses and consumers.

(3) Revision of specifications and standards for milk and milk products

Introduction

In June 2000, there were mass food poisoning outbreaks associated with low-fat milk and other milk products produced by a Japanese manufacturer. This was the most serious case in the past few decades. The Subcommittee on Food Poisoning in the Food Sanitation Committee under the Pharmaceutical Affairs and Food Sanitation

Council suggested at the session held on March 14, 2001 that the MHLW should review sanitary standards for skimmed milk powder in order to prevent the recurrence of such food poisoning. After due review, the MHLW amended the Ministerial Ordinance concerning Compositional Standards Etc. for Milk and Milk Products in December 2002 and June 2003. The following section outlines discussions at the subcommittee and the revision of standards.

Standards for manufacturing of skimmed milk powder

(a) Contamination of raw milk by *Staphylococcus aureus*.

Investigation of literature found that roughly 50% of the raw milk had been contaminated by *Staphylococcus aureus* bacteria of $10-10^3$ cfu/ml with a maximum of 10^4 cfu/ml. A few percentage points to 25 percent of the detected *Staphylococcus aureus* bacteria could produce enterotoxin A.

The subcommittee assumed that since raw milk collected from farmers was usually mixed and held in storage tanks, if raw milk from any farmer was contaminated, the contamination would spread to the whole volume. The subcommittee decided that sanitary standards should be established, on the assumption that the raw milk is already contaminated by *Staphylococcus aureus* capable of producing enterotoxin.

(b) Enterotoxin production and quantities to develop food poisoning

In laboratory tests on enterotoxin production by adding *Staphylococcus aureus* bacteria, *Staphylococcus aureus* bacteria at 10^2 cfu/ml produced enterotoxin A in six hours, and at 10^5 cfu/ml in three hours. Additional tests using concentrated milk also showed similar results.

Usually, 100 ng of enterotoxin A was known to be required to cause *Staphylococcus aureus* food poisoning in humans. In this case, food poisoning could be caused at a few tens of nanograms, according to calculation.

(c) Basic principles of sanitary standards

The subcommittee decided that sanitary standards should be based on the basic principles below.

- i. Preventive measures should be taken on the assumption that raw milk is contaminated by *Staphylococcus aureus*.
- ii. Product temperature and time during which products are kept at each temperature range should be controlled, in order to prevent the growth of *Staphylococcus aureus* in the whole course from the arrival of raw milk

through the pasteurization and concentration processes (before drying).

iii. Secondary contamination at each process should be prevented and special importance should be placed on the prevention of contamination of products after pasteurization.

(d) Sanitary standards for skimmed milk powder

Based on the above principles, the MHLW established standards including the following stipulations.

- Ingredient milk must be kept at 10°C or lower, or higher than 48°C in the process before pasteurization. However, this does not apply in the case where the manufacturing process is continuously conducted so that the ingredient milk cannot stagnate.
- Ingredient milk must be pasteurized as directed for cow's milk.
- The milk that is skimmed must be kept at 10°C or lower, or higher than 48°C in the process after pasteurization through dehydration. However, this does not apply in the case where the structure of all machines that are used in the manufacturing process can avoid contamination by the microorganisms from outside or where the product is left in temperatures over 10°C and up to 48°C for shorter than six hours.

(e) Others measures

The MHLW instructed the related businesses about the following points as well as the above-mentioned requirements.

- Raw milk should be cooled immediately after milking to 10°C or lower.
- Raw milk should be received at 10°C or lower.
- The final product (skimmed milk powder) should be stored with care, so that it cannot get damp.
- Similarly, whole milk powder, sweetened milk powder, and formulated milk powder should be handled, based on the hygienic standards above and other related instructions.

The MHLW advised ordinary consumers to store the product in a dry place, so that it cannot get damp.

Standards for pasteurization of milk and milk products

Before 2002, the Ministerial Ordinances concerning Compositional Standards etc. for Milk and Milk Products (Ministerial Ordinance No. 52, 1951) had been imposing the following standard on cow milk, pasteurized goat milk, partially skimmed milk, skimmed milk, and processed milk: Raw milk must be pasteurized at 62–65°C for 30 minutes, or by using a method providing a comparable or superior pasteurizing effect.

This stipulation was based on data on the thermal stability of *Mycobacterium tuberculosis* as an indicator. Studies conducted from 1998 to 2000 under the Health Sciences Research Program found new knowledge on contamination by Q fever of raw milk and marketed milk and lethal temperature.

(a) Lethal temperature of Q fever pathogen (*Coxiella burnetii*)

The studies confirmed that *Coxiella burnetii* died completely when heated at 65°C for 30 minutes, but some of the pathogen remained alive when heated at 62°C for 30 minutes or at 63°C for 30 minutes. When heated for 20 minutes or longer until the temperature reached 63°C, then heated at 63°C for 30 minutes, all pathogens were found to die. These results showed that 30-minute heating at 63°C using the batch method could completely kill the pathogen.

(b) Standards for pasteurization of milk

Based on the abovementioned findings, the MHLW established standards for pasteurization of milk as given bellow, in the view of the prevention of the occurrence of Q fever and global harmonization.

- Standards for manufacturing of cow milk, pasteurized goat milk, partially skimmed milk, skimmed milk, and processed milk

Raw milk must be pasteurized at 63°C for 30 minutes by the batch pasteurization or using an appropriate pasteurization method comparable or superior to this method in pasteurizing effects.

- Standards for manufacturing, processing and preparation of general foods

When a food is manufactured using raw cow milk or raw goat milk, the raw cow milk or raw goat milk must be pasteurized at 63°C for 30 minutes by the batch pasteurization or using an appropriate pasteurization method comparable or superior to this method in pasteurizing effects, during the manufacturing process.

Standards for containers and packages for milk and milk products

Standards were newly established for the following containers and packages for milk and milk products.

- Cow's milk, special milk, pasteurized goat's milk, partially-skimmed milk (low-fat milk), skim milk (nonfat milk), processed milk, and cream.
 - Laminate-form synthetic resin containers and packages using nylon
 - Laminate-form synthetic resin containers and packages using polypropylene

Nylon and polypropylene shall not be used for the surfaces coming into direct contact with the contents.

- Fermented milk, lactic acid bacterial drinks, milk drinks
 - Synthetic resin containers and packages consisting mainly of polypropylene
 - Synthetic resin containers and packages consisting mainly of polyethylene terephthalate.
- Formulated milk powder
 - Containers made by the combination of a metal can and synthetic resin laminate

(4) Standards for contaminants in food

<Standards for cadmium in rice>

(a) Standards for cadmium based on the Food Sanitation Law

In July 1970, the Ministry of Health and Welfare (the present Ministry of Health, Labour and Welfare) established the safety standard for cadmium in brawn rice at less than 1.0 ppm (less than 0.9 ppm in polished rice) based on the law, as the result of the assessment of cadmium contained in rice. Separately from regulation under the law, the National Rice Wheat and Barley Improvement Association purchases home-grown brawn rice containing 0.4 ppm or more and less than 1.0 ppm of cadmium with the support of the Japanese Ministry of Agriculture, Forestry and Fisheries and utilizes it for non-food purposes (such as starch for production of laminated wood). This is based on the decision that if brawn rice contains cadmium exceeding 0.4 ppm, the producing area may have somehow been contaminated by cadmium. MAFF's action is in consideration of consumers' sentiment.

(b) Discussion by the Joint FAO/WHO Codex Alimentarius Commission

Background

In 1998, the Codex Committee of Food Additives and Contaminants (CCFAC), a subsidiary body of the Joint FAO/WHO Codex Alimentarius Commission (CAC), proposed a draft maximum level of 0.2 ppm for cadmium in polished rice (the current draft Codex level is 0.4 ppm). Thereafter, discussions have been conducted as follows:

i. At the 36th session in March 2004, the CCFAC agreed to revise the proposed draft level for polished rice from 0.2 ppm to 0.4 ppm, based on the Japanese proposal, which was accompanied by probabilistic intake assessment data for Japanese people, and to seek CAC's judgment at step 5.¹

ii. At the 27th session in late June in 2004, the CAC asked the CCFAC to re-discuss the draft level of 0.4 ppm at step 3, in consideration of the comment from some countries that the level could result in consumption exceeding the PTWI (Provisional Tolerable Weekly Intake) ² in some regions where rice is consumed in large quantities.

iii. At the 64th session in February 2005, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) ³ concluded, as the result of the assessment of effects on the cadmium intake of three different levels (the current draft Codex level of 0.4 ppm and certain levels both above and below 0.4 ppm), that these levels would make little difference in the total intake of cadmium and would be unlikely to pose adverse effects on human health.

iv. At the 37th CCFAC session in April in 2005, many countries supported the draft level of 0.4 ppm for polished rice. Although some countries including the EU reserved its decision, the CCFAC agreed to seek CAC's judgment again at step 5.

v. At the 28th session in July 2005, the CAC adopted the draft maximum level of 0.4 ppm for polished rice at Step 5.

vi. At the 38th session in April in 2006, the CCFAC agreed to seek CAC's judgment at step 8.

vii. At the 29th session in July, the CAC adopted a draft level of 0.4 ppm and established it as the Codex standard.

Note:

1. Step (Procedure for the elaboration of Codex standards)

The procedure for the elaboration of Codex standards—in the case of cadmium, maximum level—consists of the following eight steps.

Step 1: The CAC decides to elaborate a Codex standard.

Step 2: The secretariat arranges for preparation of a proposed draft standard.

Step 3: The proposed draft standard is sent to the member countries to seek comments.

Step 4: The proposed draft standard is sent to the subsidiary body concerned to seek consideration.

Step 5: The proposed draft standard is submitted to the CAC to seek consideration on whether the proposed draft standard should be adopted as the draft standard.

Step 6: The draft standard adopted at step 5 is sent to the member countries to seek comments.

Step 7: The comments are sent to the subsidiary body concerned to seek consideration on the draft standard.

Step 8: The draft standard is submitted to the CAC to seek consideration. The draft standard is adopted as the codex standard after consideration based on the comments received.

2. PTWI (Provisional Tolerable Weekly Intake)

An estimate of the amount of a contaminant that can be ingested over a lifetime without appreciable risk, expressed as a weekly amount.

3. The Joint FAO/WHO Expert Committee on Food Additives

An international body established jointly by the Food and Agriculture Organization of the United Nations and the World Health Organization. It considers various things including the acceptable daily intake or tolerable daily intake for food additives, pesticides, veterinary drugs, and contaminants. Evaluations by the JECFA are reflected in the establishment of Codex standards.

(c) Establishment of national standards

The MHLW has asked the Food Safety Commission, which was established on July 1st, 2003, to conduct risk assessment on the assurance of food safety in light of the current situation of cadmium intakes from food. This matter is under the consideration at the special committee on contaminants.

<Standards for mycotoxins>

Mycotoxins are metabolites produced by mold. They are known to have adverse effects on humans and animals. It is very important to take appropriate measures against mycotoxins from the viewpoint of food safety. In recent years, some cases of acute poisoning of livestock have been reported. These circumstances require adequate measures to protect human health.

In recent years, the world has come to recognize the seriousness of the contamination of mycotoxins. The CAC has conducted lively discussion on mycotoxins in food, and established Codex standards for some micotoxins. In response to a request of

the CAC, the JECFA conducted safety evaluation on various mycotoxins in February 2001. It is expected that approaches towards the development of standards will accelerate in the near future.

Establishment of standards in Japan

Basically, standards are established through in-depth discussion at the Food Safety Commission and the Pharmaceutical Affairs and Food Sanitation Council. First, the Commission conducts toxicity evaluation based on evaluations by the JECFA and establishes the no-observed-effect level (NOEL)¹ or no-observed-adverse-effect level (NOAEL)² for each mycotoxin. Then, the Commission determines the tolerable daily intake (TDI) by applying appropriate safety factors.³ In light of the evaluation by the Commission, the Council establishes standard limits for individual foods. In the standard setting, the Council takes account of food consumption, loss during food preparation, and Codex standards. Standard limits are established so that the sum of limits on individual foods for a mycotoxin does not exceed the tolerable daily intake (TDI).⁴

Notes:

1. No-Observed Effect Level (NOEL)
The highest dose of a substance that does not cause any changes distinguishable from those observed in normal animals.
2. No-Observed-Adverse-Effect Level (NOAEL)
The highest dose of a substance at which does not cause any detectable toxic effects in experimental animals.
3. Safety factor
A factor that is obtained, considering inter-species variability in between experimental animals, intra-species variability between humans, and other conditions.
4. Tolerable Daily Intake (TDI)
An estimate of the amount of a contaminant that can be ingested daily over a lifetime without appreciable risk.

(a) Discussion on the establishment of standards for deoxynivalenol

i. Deoxynivalenol (DON) is a mycotoxin produced by fungi of genus *Fusarium*. It contaminates cereal grains, like barley, wheat, and oats. This family of fungi causes *Fusarium* head blight in barley when a humid climate, like rainy season, coincides with the timing of flowering-to-maturing. The DON poisoning of humans is characterized by gastrointestinal symptoms such as nausea, vomiting, and diarrhea. In dosing tests in mice, effects on thymus, spleen, heart, and liver were reported. DON is highly thermo-stable and is not reduced in ordinary cooking

processes.

ii. The MHLW conducted an investigation to identify the contamination of grains with DON in 2001, and considerably high levels of DON were detected in some samples. The following are investigation results.

iii. The Joint Subcommittee of Food Standards and Toxicity under the Pharmaceutical Affairs and Food Sanitation Council discussed, in May 2002, whether standards for DON should be established.

iv. The Joint Subcommittee concluded that standards under Article 11 of the law* were necessary to reduce health risk from the intake of DON and to prevent health hazards. The Subcommittee stated that a guideline level of 1.1 ppm should be applied for wheat until the standard is set.

v. The Joint Subcommittee concluded at a meeting held in 2003 that additional investigations targeted at wheat, household-use wheat flour, and baby foods were necessary to obtain enough data for establishing standards. The subcommittee mentioned that investigations for wheat should be focused on yearly changes in DON concentration in crops. The MHLW will establish standards after the results of additional investigations become available, taking discussion by the CAC into account.

(b) Establishment of standards for patulin in apple juice

i. Patulin is a mycotoxin produced by certain fungi of the genera *Aspergillus* and *Penicillium*. This mycotoxin is usually found in foods that are contaminated by these fungi, including fruits, vegetables, cereal grains, and animal feed. Apple juice is known to be a food that is most likely to be contaminated by patulin.

ii. A national investigation conducted in fiscal 2002 on patulin contamination in apple juice showed that the mycotoxin was detected in some samples at as high levels as those that become targets of regulation in other countries.

iii. In response to the result, the Joint Subcommittee discussed the establishment of standards for patulin in December 2002.

iv. The joint subcommittee concluded that the standards given below should be established under Article 11 of the law in order to prevent health hazards by reducing health risk occurring through patulin consumption and to harmonize with international standards.

* Provisions of the Food Sanitation Law that appear in this text are given in Annex 8 to Part I *Administration of Food Safety*.

Standard: Patulin concentration must not exceed 50 ppb in apple juice and apple juice ingredients for other nonalcoholic beverages.

v. The MHLW will investigate the state of contamination to identify effects on subpopulations such as young children. The MHLW will review the established standards if it determines that the action is necessary based on evaluation by the CAC.

2. Pesticide Residues in Food

(1) Historical background

In 1956, residue limits for pesticides were established for the first time in Japan, coinciding with a rapid increase in the use of pesticides after the war. These limits were set for arsenic, lead, copper, and DDT on apples.

However, it is not until 1968 that maximum residue limits (MRLs) for pesticides were established under the Food Sanitation Law. MRLs were established for five pesticides (arsenic, BHC, DDT, lead, and parathion) on four crops (apple, cucumber, grape, and tomato).

By 1978, the number of pesticides with MRLs had increased to 26 substances. Thereafter until 1991, no MRLs were established.

After 1991, MRLs have been established annually for several pesticides on individual agricultural commodities. By the end of 2005, MRLs were established for 250 pesticides.

In 2003, the law to amend the Food Sanitation Law required the introduction of a positive list system for regulation of agricultural chemicals (pesticides, veterinary drugs and feed additives).

On May 29, 2006, the positive list system took effect.

(2) Relationship between the registration of pesticides and the regulations on pesticide residues in foods (mainly concerning responsibilities of the three ministries)

In Japan, three major laws are related to the regulation of pesticides. These laws are the Agricultural Chemical Regulation Law (ACRL), the Food Sanitation Law (FSL), and the Food Safety Basic Law (FSBL), which was enacted in May 2003. The ACRL, the FSL, and the FSBL are under the control of the Ministry of Agriculture, Forestry and Fisheries, the Ministry of Health, Labour and Welfare, and the Cabinet Office, respectively.

All pesticides including imports must be registered under the ACRL before they can be used or sold in Japan. MAFF is responsible for the registration of pesticides. Before a pesticide is registered, MAFF will discuss the adequacy of approval of the pesticide. The discussions include the physical nature and the effectiveness of the pesticide. In addition, the ACRL requires the Ministry of Environment to discuss the environmental effects of the target pesticide, such as those of residues in foods and feeds on humans, animals, soil, and water.

Health risk assessment is conducted by the Food Safety Commission, which was established under the FSBL in July 2003. The commission establishes the ADI (Acceptable Daily Intake)*. The MHLW establishes MRLs for the pesticide, taking into consideration the risk assessment result reported by the commission.

Annex 1 outlines the responsibilities of the MHLW, the Ministry of Agriculture, Forestry, and Fisheries, and the Ministry of the Environment under the three laws.

Note:

ADI (Acceptable Daily Intake)

An estimate of the amount of a substance that can be ingested daily over lifetime without appreciable health risk, usually expressed on a body weight basis (mg/kg/day).

(3) Legal nature of pesticide residue standards

Article 11, Paragraph 1 of the Food Sanitation Law stipulates that the Minister of Health, Labour, and Welfare may establish specifications for components of foods to protect the public health. The law treats pesticide residues as part of components of foods. Pesticide residue standards are usually called maximum residues limits, or MRLs. They refer to the maximum concentrations that may remain in or on target commodities. Foods containing pesticides above the MRLs are enjoined from domestic distribution and import.

Before the implementation of the positive list system, crops containing pesticides without MRLs were not under the control of Article 11 of the law and could be distributed in the domestic market unless they posed health hazards to humans under the meaning of Article 6 of the law.

Based on the 2003 amendment of the law, on May 29, 2006 the MHLW implemented the positive list system for pesticide residue regulation. Under the system, any food that contains a pesticide without residue standards is basically enjoined from domestic distribution. Pesticides, however, may remain in foods as long as residue levels are below a certain level that is determined to pose no adverse health effects. A similar system is already being carried out in other countries, like Australia, Germany, and the United States.

As of the end of 2005, the number of chemicals with MRLs was 250 in Japan. On the other hand, some 700 pesticides were in use in the world for food-use crops. Therefore, the MHLW provisionally established MRLs (provisional MRLs) for pesticides without MRLs for individual foods. In setting provisional MRLs, the MHLW took into consideration Codex standards and other standards that were based on scientific evaluation. The newly established MRLs became effective along with the positive list system on May 29, 2006. Basically, provisional MRLs and existing MRLs are equally treated under the law. Consult Annex 2 (which illustrates the previous system and the positive list system) and Appendix to Annex 2 (which outlines the establishment of provisional MRLs).

The MHLW plans to have the Commission conduct safety assessment of chemicals for which provisional MRLs have been established. In light of the assessment results, the MHLW will review provisional MRLs as required.

The effective MRLs, including the provisional MRLs, are available at

http://www.mhlw.go.jp/english/topics/food_safety/positovelist060228/index.html

(4) Establishment of MRLs for pesticides

Related laws have been amended in step with the enactment of the Food Safety Basic Law in May 2003. This has enabled the MHLW to establish MRLs for pesticides at the time of registration by the Ministry of Agriculture, Forestry and Fisheries.

The establishment of an MRL begins with the submission of an application for registration to the Ministry of Agriculture Forestry and Fisheries (see Annex 3). Upon receiving notification from MAFF of the application, the MHLW will request MAFF to provide the documents required for safety evaluation under Article 12 of the law. These documents include acute toxicity, subacute toxicity, chronic toxicity, carcinogenicity, reproductive toxicity, teratogenicity, genetic toxicity, pharmacokinetic and general pharmacological parameters, animal metabolism, and plant metabolism as well as residue data for commodities treated with target pesticides.

The MHLW will ask the Commission for opinions concerning health effects after obtaining the necessary documents. In response to the consultation, the commission will conduct a health risk assessment and establish the ADI (Acceptable Daily Intake). In establishing the ADI, the NOAEL (No-Observed-Adverse-Effect Level),¹ which is basically determined from animal studies, and the safety factor ² are used. The MHLW will have the Pharmaceutical Affairs and Food Sanitation Council establish MRLs. MRLs will be established based on an exposure assessment, using the ADI established by the Commission.

Currently, Japan uses the theoretical maximum daily intake (TMDI) method and estimated daily intake (EDI) method for the exposure assessment (see Annex 4). The MRLs for a pesticide are allocated to individual foods so that the calculated daily intake of the pesticide does not exceed its ADI. Residue data obtained from field trials in which the pesticide was used in accordance with the use direction claimed at registration application are the basis for the MRL on the target crops.

When the commission determines that no ADI can be set for a pesticide, the MRL will be established for the pesticide as N.D. (no detection) meaning the limit-of-detection level.

The process of establishing MRLs for pesticide is described in Annex 3.

Notes:

1. NOAEL (No-Observed-Adverse-Effect Level)

2. Safety factor

See the Section 4 “Standards for mycotoxins in food” under the heading of “1. Food.”

(5) Harmonization with Codex standards (international standards)

The SPS (Sanitary and Phytosanitary) Agreement of the WTO Agreement requires each member country to harmonize its food safety regulations with international regulations, in order to minimize the impact of discrepancies in regulation between member countries on trade. Based on this principle, Japan accepts Codex standards as far as possible when establishing MRLs, as long as the acceptance is unlikely to pose a major problem.

(6) Investigation of pesticide residues in food

Monitoring tests

Monitoring tests target pesticides with MRLs. The purpose of monitoring tests is to check whether agricultural products in the marketplace comply with the established MRLs. Quarantine stations and local governments are responsible for monitoring tests. Quarantine stations monitor imported products, and local governments monitor products on the domestic marketplace.

Products that do not meet the standards will be recalled, discarded, reshipped, or otherwise disposed of.

(7) Survey of pesticide intakes (Market Basket Study)

Then Ministry of Health and Welfare started to conduct surveys on pesticide intakes (Market Basket Method) in 1991, in order to estimate intakes of pesticides through the daily diet. These surveys may enable more precise estimation of the intake of pesticides, since samples are prepared/cooked before analysis as they would be normally. Most of the pesticides remaining in or on foods are assumed to be reduced, removed, or degraded through preparation processes such as washing, peeling, cutting, boiling, frying, and steaming.

The survey results determined that dietary intake is unlikely to pose health problems in the current situation, because the estimated intakes were well below the corresponding ADIs.

In 1991–2003, 160 pesticides were tested, and 28 pesticides out of them were detected in one of the food groups tested. The 28 include DDT, azinphos-methyl, acephate, chlorpyrifos, fenvalerate, and malathion. The estimated daily intakes of pesticides detected were in general way below the corresponding ADIs, except for bromine, which naturally occurs. Even some estimated daily intakes that were considerably large were about 27% of the corresponding ADIs.

(8) Information disclosure

Summary results of evaluation by the Council, and monitoring tests are made public on the MHLW web site. Also, results of pesticide residue surveys and total diet studies are published in writing.

3. Veterinary Drugs (including Feed Additives) in Food

(1) Historical background

Veterinary drugs are used to prevent and treat illnesses of livestock, such as cows and pigs, poultry, and finfish/shellfish. These drugs include chemically-synthetic antimicrobials, antibiotics, and anthelmintics. Feed additives are added to feed mainly for preventing feed quality.

The Food Sanitation Law stipulates that in principle, foods must not contain antibiotics. It also stipulates that in principle, meat, fowl eggs, and fish and shellfish must not contain chemically synthesized antimicrobials. These provisions were established, considering problems with the safety of these drugs and health effects of drug-resistant microorganisms, which may appear as a result of the use of these drugs. The law permits foods to contain these drugs only when the drugs comply with individual standards established under the law.

In December 1995, Japan established first residue standards for veterinary drugs (six substances). By the end of 2005, standards were set for 33 drugs. The following shows the breakdown:

- Antibiotics and chemically synthesized antimicrobials 17 items
- Anthelmintics 13 items
- Hormones 2 items
- Feed additive 1 item

As mentioned in section 2 (1) of this document, veterinary drugs are also subject to the positive list system for regulation of agricultural chemicals (effective on May 29, 2006).

Related laws have been amended in the wake of the May 2003 enactment of the Food Safety Basic Law. This enabled the MHLW to establish residue standards for veterinary drugs and feed additives at the time when MAFF approves these drugs or designates feed additives.

(2) Establishment of residue standards (MRLs)

Process of establishment of MRLs

Basically, MRLs for veterinary drugs are established in the same manner as for those for pesticide residues. Please consult section 4 “Establishment of MRLs for pesticides.” In this section an outlined is just given.

First, the Food Safety Commission conducts a health risk assessment of target substances. During the risk assessment the NOEL (No-Observed Effect Level) ¹ or the NOAEL (No-Observed-Adverse-Effect-Level) ² is established using results of several toxicity studies including chronic study, teratotoxicity study, and carcinogenicity study.

Second, the ADI (Acceptable Daily Intake) ³ is obtained by multiplying the NOEL/NOAEL by the safety factors. For antibiotics and chemically synthesized antimicrobials, the microbiological ADI is also taken into account in order to consider effects on human intestinal flora.

Third, MRLs are set, taking residue data and Codex standards into consideration.

Then, the TMDI (Theoretical Maximum Daily Intake) is obtained using the MRLs and the total intake of the target foods (based on the National Nutrition Survey). When it is confirmed that the TMDI is less than the ADI and that there is no specific problem, the MRLs are adopted. (Annex 4)

The positive list system was also implemented for veterinary drugs and feed additives. Basically, the system prohibits any food that contains a drug or feed additive without residue standards from being distributed in the domestic market. These drugs or additives, however, may remain in foods as long as residue levels are below a certain level that is determined to pose no adverse health effects. This provision does not apply to antibiotics and antimicrobials even after the implementation of the system.

Given veterinary drugs and related chemicals that are distributed abroad, the MHLW provisionally established residue limits for substances whose safety were confirmed at certain levels in the same manner as for pesticides residues. The newly established limits became effective on the date of the enforcement of the system. See Appendix 4. Registration withholding limits are not established for veterinary drugs and feed additives. The effective MRLs, including the provisional MRLs, are available at http://www.mhlw.go.jp/english/topics/food_safety/positovelist060228/index.html

Notes:

1. NOEL (No-Observed Effect Level)

2. NOEEL (No-Observed-Adverse-Effect-Level)

3. ADI (Acceptable Daily Intake)

See the section “4. Standards for mycotoxins in food” under the heading of “I. Food.”

(3) Investigation of veterinary drugs in foods

Monitoring tests

Veterinary drugs are monitored in the same manner as for pesticides residues. Monitoring tests target drugs with MRLs. Food products that do not meet the standards will be recalled, discarded, reshipped, or otherwise disposed of.

(4) Information disclosure

Summary results of safety evaluations by the Pharmaceutical Affairs and Food Sanitation Council and monitoring test results are made public on the MHLW website.

4. Food Additives

(1) Historical background

In 1947, then Ministry of Health and Welfare enacted the Food Sanitation Law as the first comprehensive law for food safety/hygiene, and introduced a positive list system for food additives. Under the system, only food additives designated as safe by the Minister of Health, Labor and Welfare may be used in foods. Since 1947, all food additives have been regulated by this law. However, designation system had been applied only to chemically synthesized food additives until 1995 when the law was amended. Currently, all food additives are equally subject to the designation system, synthetic or non-synthetic, with minor exceptions.

(2) Regulation of food additives under the Food Sanitation Law

(a) Definition of “food additive”

The law, in the first Chapter, defines “food additive” as

- i. substances used in or on food in the process of manufacturing food, or
- ii. substances used for the purpose of processing or preserving food.

Consequently, “food additive” includes both substances remaining in the finished food products, such as food colors and preservatives, and substances not remaining in the finished products, such as infiltration-supporting agents.

(b) Designation of food additives

Designation of a food additive is normally in accordance with the procedure given below, based on an application from a person who wishes to use it.

When an application for designation of a food additive is submitted to the Minister, the Minister will ask the Food Safety Commission for opinions concerning health effects of the food additive. At the request for opinion, the necessary documents obtained are submitted to the commission. The Commission will make a scientific health risk assessment and establish the ADI. After the MHLW receives the Commission’s report and recommendation, it will have the Pharmaceutical Affairs and Food Sanitation Council discuss the adequacy of draft standards. In discussion by the Council, international evaluations were taken into account. If the discussion proves that the food additive is safe and effective, it will be designated as a food additive approved for use.

Documents accompanying an application should comply with the directions given in the “guidelines for designation of food additives and for revision of standards for use of food additives.” The safety and effectiveness of a food additive must be scientifically confirmed (see Annex 5).

As of the end of July 360 food additives were designated as approved by the Minister of Health, Labour and Welfare under Article 10 of the law (see Annex 6).

Separately from the designation process described above, the MHLW evaluates certain food additives with intent to designate them without any application from a person who wishes to use them. This program targets substances that meet the standards given below. This program aims to take internationally harmonized measure for substances that are proven safe and widely used abroad. This action underlies the following background. In recent years, global food trade has been expanding, and imported foods account for some 60 percent of the foods distributed in the Japanese market. In addition, there is a growing possibility that imported foods contain food additives that are authorized in other countries but unauthorized in Japan.

Currently, 46 substances and some flavoring agents are targeted by the program. Discussion is being conducted on substances for which the full documents on safety and usefulness are prepared.

Standards

Substances:

- for which a safety assessment has been finished by the JECFA (Joint FAO/WHO Expert Committee on Food Additives) and whose safety has been confirmed within a certain level, and
- that are widely used in the United States and EU countries and whose necessity is considered to be high.

Exemption from the designation system

There are three substance categories that are exempted from the designation system.

- i. Existing food additives (i.e., substances that were already marketed or used on the date of the amendment of the law and appear in the List of Existing Food Additives).
- ii. Natural flavoring agents.
- iii. Substances that are both generally provided for eating or drinking as foods and used as food additives have been excluded from the designation system.

(c) Establishment of specifications and standards

Usually, people continue to consume food additives throughout their lifetime. Thus, food additives must be subjected to stringent regulations.

All designated chemicals, with a few exceptions, and some natural food

additives (existing food additives) are currently regulated by specifications and/or standards. These specifications and standards include specifications concerning chemical and physical characteristics, and standards for manufacturing, storage, and use. These standards, along with labeling and storage standards, are published in an official compilation of food additives, entitled “*Japan’s Specifications and Standards for Food Additives.*”

(d) Official compilation of food additives

In 1957, the law was amended, and a provision about an official compilation of food additives was newly established in order to collect the specifications and standards for food additives. Based on this provision, then Minister of Health and Welfare, on March 15, 1960, prepared the first edition of an official compilation of food additives.

Since the first edition was published, the publication has been updated periodically to keep pace with scientific advances and harmonize Japanese standards with international ones. The latest edition (seventh) was published in April 1999. Its English translation was published in September 2000. The MHLW is working to prepare the eighth edition.

(e) Food additive labeling

Labeling of food additives and their preparations

Any food additive and its preparations intended for sale in Japan must be labeled with required information as prescribed in the law. The information includes product name, manufacturer’s name, the address of the manufacturing plant, and standards for use.

Labeling of food containing food additives

The law requires all foods containing food additives, with some exceptions, to be labeled with the substance name without discriminating between synthetic and nonsynthetic (so-called natural).

Before the current enforcement regulations under the law came into effect in July 1991, only certain kinds of synthetic chemicals had been subject to labeling regulations. However, due partly to consumers' requests, the current labeling system was established. This was based on the conclusion that the declaration of every food additive used in food would be necessary to provide consumers with important information in choosing food.

In principle, the substance names used for labeling should be individual chemical names, but widely used common names may be used as well. Any food

additive used for one of the eight usages (as sweetener, food color, preservative, thickening agent, antioxidant, color fixative, bleaching agent, fungicide) must be labeled with the name of that usage as well as with its chemical name, for example, preservative (Sorbic Acid). In addition, any food additive used for one of 14 specific usages, such as flavoring and pH regulation, may be exempted from the labeling with its substance name, and may be labeled only with the name of that usage; e.g., flavoring agent, pH regulator.

(f) Product examination of food additives

Official examination

The law requires certain food additives to undergo official examination. The examination system targets food additives that require legal quality control to assure the safety. Under the current regulations, only tar colors are subject to the system. Products that have passed the examinations are given certificates.

Voluntary certification system

Separately from the official examination system mentioned above, the additive industry operates a voluntary certification system. The system applies to *Kansui* (alkali), which are used in Chinese noodles, and tar color preparations. Examinations are conducted by public laboratories or registered laboratories (those registered with the Minister). The Japanese Food Additives Association issues a certificate to products that have passed the examinations.

(3) International safety assessment of food additives

Most countries are commonly interested in securing food safety and improving consumer's health. The Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) have jointly established the Joint FAO/WHO Expert Committee on Food Additives (JECFA) to evaluate the safety of food additives. The JECFA is comprised of experts in food additive standards and toxicologists from various countries. They evaluate the results of safety tests conducted by individual countries and determine the acceptable daily intake (ADI) of each of the additives for which data are sufficiently accumulated and that are proved to be safe for human consumption. The report of each JECFA meeting is publicized in the WHO Technical Report Series every year.

(4) Safety measures for non-synthetic food additives

Non-synthetic food additives have been regulated in the same manner as synthetic

chemicals since May 24, 1996, to assure the safety of such food additives. However, non-synthetic food additives (450 existing food additives as of July 1, 2006), which were already distributed before the amendment of the law, have been permitted for free distribution even after May 24, 1996. Such food additives are not subject to Article 6 of the amended law.

The MHLW is working to confirm the safety of these substances by conducting toxicity studies or examining related literature.

As part of its safety program, the MHLW is working to establish quality specifications, taking into consideration harmonization with international specifications.

The 2003 amendment of the law has enabled the MHLW to prohibit the use of existing food additives by deleting them out of the list of existing food additives, when they are considered to be fall into one of the following categories.

Target substances

- i. Those that are considered to have problem with safety.
- ii. Those that are no longer in use.

Based on the amended law, the MHLW published in February 2004 a list of 38 existing food additives, which were no longer in use. In July 2004 the MHLW delisted madder color—a coloring agent obtained from plant root—and prohibited its use in food. This action was taken in response to the interim report of a carcinogenicity study that found madder color to be carcinogenic to the rat kidney. Before the action was taken, the MHLW took into account discussions by the Commission and Pharmaceutical Affairs and Food Sanitation Council. The abovementioned 38 substances were delisted in December to prohibit their use.

(5) Survey of daily intakes of food additives

Survey of daily intakes of food additives is one of the most important programs concerning food additive safety. The MHLW estimates the dietary intakes of food additives by the Market Basket Survey.

The Market Basket Survey is conducted by purchasing foods distributed on the marketplace, analyzing food additives included in these foods, and determining each amount in individual foods. Then, the total intake per capita of a target food additive is estimated by multiplying the obtained amount by the consumption of the corresponding food and obtaining the sum of all intakes for the target foods.

The 10-year study report (1976–1985) and the latest study result (1999, 2002, and 2003) concerning daily intakes of food additives shows that the per capita intake of each food additive is below its ADI.

5. Apparatus and Containers/Packages, Toys

<Apparatus and Containers/Packages>

(1) Historical background

Legal control over apparatus and containers/packages began from the standpoint of food safety in step with the enactment of the Food Sanitation Law in December 1947. In 1948, first standards and specifications for food, food additives, apparatus and containers/packages were established under the law. In 1959, the existing standards and specifications were withdrawn and replaced by integrated ones including testing methods (Ministry of Health and Welfare Notification No. 370).

To this date, there have been several establishments and revisions of standards and specifications.

(2) Definitions

All apparatus and containers/packages that come into direct contact with foods are subject to regulation of the law. "Apparatus" means articles used for manufacturing, processing, preparing, storing, transporting, or otherwise handling foods. "Containers/packages" means articles used for wrapping and packing foods for delivering. Apparatus and containers/packages include a wide variety of articles such as kitchen utensils, gloves for food-handling, tableware, and wrapping film.

(3) Establishment of Specifications and Standards

The specifications for apparatus and containers/packages are divided into three categories: a) specifications applying generally to apparatus and containers/packages and their raw materials, b) specifications for apparatus and containers/packages by material and c) specifications for apparatus and containers/packages by use. The standards are established for manufacturing.

(a) Specifications applying generally to apparatus and containers/packages and their raw materials

These specifications apply to mainly metals and colors used as materials/ingredients of products. The metals include tin for plating, solder, and products containing copper, lead, or antimony.

The specification for colors applies to all products. Coloring agents used for apparatus and containers/packages must be food colors designated by the Minister of Health and Welfare under Article 10 of the law. However, this does not apply where target products are processed in an appropriate way so that no color may

dissolve or migrate in foods.

The MHLW newly established specifications for apparatus, containers, and packages that are intended for edible fats or oils or oily foods in August 2002 and put them into force in August 2003. Polyvinylchloride resins containing di(2-ethylhexyl) phthalate (DEHP) must not be used as materials of apparatus, containers, and packages for these foods. Any person is prohibited from marketing or using these PVC products containing DEHP.

(b) Specifications for apparatus and containers/packages by material

These specifications target six material categories: glass, ceramics, enamel, 11 types of synthetic resins, rubber, and metal. There are no specific specifications for products made of paper or wood, which are subject to Article 9 of the law in the same manner for other apparatus and containers/packages. Based on Article 9, any product is enjoined from manufacture, sale, and use, when determined to be toxic or harmful.

These specifications consist of material tests and migration tests. Material tests aim to determine constituents derived from raw materials used. The test items include metals (e.g., cadmium and lead) and volatile substances.

Migration tests aim to determine amounts of substances that dissolve in solutions meeting the specified conditions, from different facets. These tests include various items, such as residues on evaporation, heavy metals, consumption of potassium permanganate. For individual specifications, consult the separate document (*Specifications and Standards for Foods, Food Additives, etc. under the Food Sanitation Law: Abstracts*).

(c) Specifications for apparatus and containers/packages by use

The law also provides specifications for products by use. These specifications include necessary requirements according to purposes of use. The specifications include strength tests, such as water leak tests and pinhole tests.

The following are product categories by use:

- i. Containers and packages for foods that are packed into containers and pasteurized under pressure
- ii. Containers and packages for nonalcoholic beverages
- iii. Food-vending machines and containers that accompany a vending machine and with which the food is sold
- iv. Apparatus that are used for manufacturing edible ices or for other uses of edible ices

- v. Apparatus or containers/packages that are used for delivery of concentrates of nonalcoholic beverages for cup-unit vending machines or full-automatic nonalcoholic-beverage preparing machines

<Toys>

The law applies to toys designated by the Minister as those that may pose health hazards to young children through direct contact with the mouth. Young children normally refer to those of preschool age. The law establishes specifications and standards for toys. They include specifications for toy products and raw ingredients and standards for manufacturing.

(1) Specifications for toys and raw ingredients

The specifications apply to toy products themselves (rub-on pictures and *origami* paper, or folding paper) and raw ingredients (polyvinyl chloride paints, materials consisting mainly of PVC, and materials consisting mainly of polyethylene). Rubber pacifiers are also subject to specifications.

In August 2002, specifications were newly established for toy ingredients as well as for plastic apparatus and containers. PVC resins containing DEHP must not be used as toy ingredients. In addition, PVC resins containing diisononyl phthalate (DINP) must not be used as ingredients of certain types of toys (i.e., toys intended to come into direct contact with the mouth of young children, including pacifiers and teething rings). Any person is prohibited from marketing or using PVC toy products containing DEHP or DINP.

(2) Standards for manufacturing

The law regulates coloring agents used for toys. If toys are painted with synthetic coloring agents, the agents must be food colors designated by the Minister based on Article 10 of the law. However, this requirement does not apply to the case where the coloring agents do not dissolve in the test specified by Ministry of Health and Welfare Notification, No 370, 1959.

6. Food labeling

(1) In general

Food, food additives, and apparatus, and containers/packages with intent to sell are required to be labeled with information as specified under the Food Sanitation Law from the viewpoint of public health. The required information includes substance name, best-before date, ways of storing, and manufacturer. Any food containing food additives must be basically labeled with the names of all food additives included in it.

(2) Labeling of allergenic substances in foods

On April 1, 2001, labeling provisions for foods containing allergenic substances came into effect, based on the law. These provisions require certain types of food ingredients to be declared. In the recent years, many health hazards associated with foods containing allergenic substances have been identified. The allergy labeling aims to provide consumers with necessary information, in order to prevent potential health risks.

The allergy labeling targets packed processed foods containing 25 types of products given below. These 25 are categorized into two groups: 1) foods that can cause severe allergic symptoms and on which the yearly number of cases is large, 2) foods which can cause health hazards but on which the yearly number of cases is small. The Ministerial Ordinance requires the five foods categorized into group 1 to be labeled. For the remaining 20 foods categorized into group 2, labeling is recommended by the Department of Food Safety Notice but not compulsory.

- Five foods for which labeling is compulsory
Buckwheat, eggs, milk, peanuts, and wheat.
- Twenty foods for which labeling is recommended
Abalone, apple, banana, beef, chicken, crabs, gelatin, kiwifruits, mackerel, *matsutake*-mushroom, oranges, peach, pork, prawn, salmon, salmon roes, soybeans, squid, yam, walnuts.

The MHLW is reviewing the labeling system for allergenic substances.

(3) Labeling of genetically modified foods

In April 2001, the labeling for genetically modified foods became mandatory in Japan. The labeling is under the jurisdiction of two ministries: the Ministry of Agriculture, Forestry and Fisheries and the Ministry of Health, Labour and Welfare. MAFF intends to provide consumers with information in choosing food under the Japanese Agricultural Standards Law. The MHLW intends to publicize the fact that the

product has undergone the safety assessment. Currently, the safety assessment is mandatory under the law and only genetically modified foods that have undergone the safety assessment may be distributed in the domestic market. The labeling is part of the legal safety assessment system under the law.

The labeling should be as follows:

- i. Genetically modified crops, and their processed foods: A statement to the effect that this is a genetically modified food (mandatory labeling)
- ii. Crops that have not been separated from genetically modified crops and that might include genetically modified crops, and their processed foods: A statement to the effect that this is a non-separated food (mandatory labeling)
- iii. Non-genetically modified crops that have completely been separated from genetically modified crops, and their processed foods: A statement to the effect that this is a non-genetically modified food (voluntary labeling)

Foods that require labeling:

- Crops
Soybeans, corns, rape seeds, potatoes, cotton seeds, and alfalfa
- Processed foods (As of April 2004)
 1. *Tofu* (soybean curd) and fried *Tofu*.
 2. Frozen *Tofu*, *Okara* (bean curd refuse), and *Yuba* (film-formed products obtained by heating soybean milk).
 3. *Natto* (fermented soybeans).
 4. Soybean milk and its similar products.
 5. *Miso* (fermented soybean paste: seasoning).
 6. Simmered soybeans.
 7. Canned and bottled soybeans.
 8. Soybean flour.
 9. Roasted soybeans.
 10. Products that are made mainly of foods listed in 1 through 9.
 11. Products that are made mainly of soybeans, excluding foods listed in sections 1 through 11.
 12. Products that are made mainly of soybean flour.
 13. Products that are made mainly of soybean protein.
 14. Products that are made mainly of succulent soybeans.
 15. Products that are made mainly of soybean sprouts.
 16. Savory that are made mainly of corns.
 17. Corn starch.
 18. Pop corns.
 19. Frozen corns.
 20. Canned and bottled corns.
 21. Products that are made mainly of corn flour.
 22. Products that are made mainly of corn grits.
 23. Products that are made mainly of corns, excluding foods listed in 16 through 22.
 24. Products that are made mainly of foods listed in 16 through 20.
 25. Frozen potatoes.
 26. Dry potatoes.
 27. Potato powder.
 28. Savory made of potatoes.
 29. Products that are made mainly of foods listed in 25 through 28.
 30. Products that are made mainly of potatoes, excluding foods listed in 25 through 29.
 31. Products

that are made mainly of alfalfa.

Processed foods given below are exempted from mandatory labeling and can be labeled voluntarily.

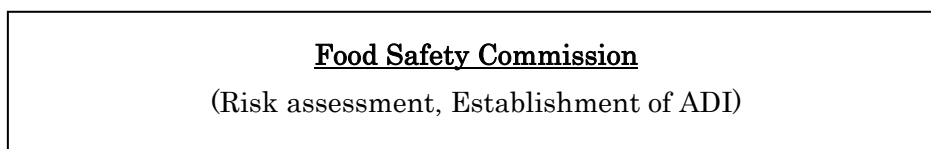
- Products from which recombinant DNA and protein are removed.
- Products in which the crops listed above are not used as major ingredients (“major ingredients” refers to the three major ingredients of the product in terms of weight, and the proportion of each ingredient is 5% or more by weight).

Annexes

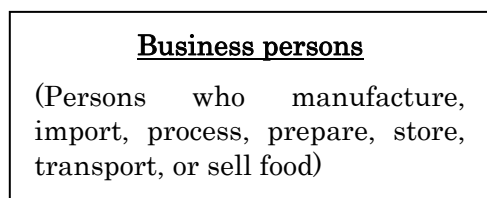
1. Regulatory status on pesticide residues by the Food Safety Basic Law, the Food Sanitation Law, and the Agricultural Chemicals Regulation Law
2. Positive List System for Agricultural Chemical Residues
 Appendix Implementation of the positive list system for agricultural chemical residues in foods
3. Pesticide Registration and Establishment of MRLs
4. Basic principles for establishment of maximum residue limits for pesticides in agricultural products (including Diagram)
5. Guidelines for designation of food additives, and for revision of standards for use of food additives (excerpt) (including table and diagram)
6. Change in the number of designated food additives

Regulatory Status on Pesticide Residues under the Food Safety Basic Law, the Food Sanitation Law, and the Agricultural Chemicals Regulation Law

[Food Safety Basic Law]



[Food Sanitation Law]



Business license

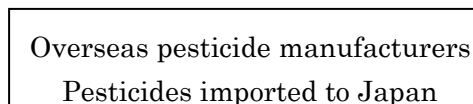
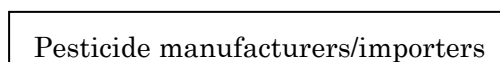
Collection
Food inspection
Disposal order

Ministry of Health, Labour and Welfare

- * Establishment of standards/specifications for food (Residue standards: MRLs)
Prevention of health hazards arising from food consumption
- * Prohibition of sale/import of food in violation of standards

Pharmaceutical Affairs and Food Sanitation Council

[Agricultural Chemicals Regulation Law]



Application for registration
(Accompanying data on efficacy, toxicity, residue property, etc.)

Ministry of Agriculture, Forestry and Fisheries

- * Pesticide registration
- * Labeling regulation of pesticides
- * Establishment of use standards for pesticides
- * Sales control/prohibition of pesticides
- * Cancellation of pesticide registration

Agricultural Material Council

Ministry of the Environment

Establishment of registration withholding limit (RWL)

Note: The Food Sanitation Law prohibits the distribution of foods that do not meet the MRLs. The Agricultural Chemicals Regulation Law prohibits the registration of pesticides that do not meet the RWLs. The MRLs established by the MHLW are also used as RWLs.

Implementation of the Positive List System for Agricultural Chemical Residues in Foods

I. Introduction of the positive list system

On May 29, 2006 the Ministry of Health, Labour and Welfare (MHLW) introduced the positive list system for agricultural chemicals remaining in foods—a system to prohibit the distribution of foods that contain agricultural chemicals above a certain level if maximum residue limits (MRLs) have not been established. The agricultural chemicals include pesticides, feed additives and veterinary drugs. This activity has been based on the Law to Partially Amend the Food Sanitation Law (Law No. 55, 2003). The Law No. 55 has required the MHLW to take the following measures within three years after the publication of the amended Food Sanitation Law (May 30, 2003).

Measures the Law required the MHLW to take

- i. To establish a certain limit stipulated in Article 11 Paragraph 3 of the amended Food Sanitation Law* as a limit that is unlikely to pose adverse health effects (hereinafter referred to as the “uniform limit”)
- ii. To designate substances stipulated in Article 11 Paragraph 3 of the amended FSL as those that will not pose adverse health effects (hereinafter referred to as “exempted substances”)
- iii. To establish maximum residue limits stipulated in Article 11 Paragraph 1 of the FSL, which are provisionally established as compositional specifications for food (hereinafter referred to as “provisional MRLs”)—as maximum levels of chemicals that can remain in foods—in order to protect public health and smoothly implement the positive list system.

II. Specifics of uniform limit, exempted substances, and provisional MRLs

A. Uniform limit

The uniform limit has been established for agricultural chemicals without MRLs. Basically, before a chemical is authorized, discussions are conducted on toxicity and other necessary matters. Based on the discussion results, restrictions are set on target crops and use amounts. Also, applications to the target crops and maximum limits that can remain in foods are established. This activity is conducted in the similar manner, regardless of country.

* Article 11 Paragraph 3 was newly added based on the Law to Partially Amend the Food Sanitation Law (Law No. 55, 2003). The added provision took effect on May 29, 2006.

Appendix to Annex 2

The MHLW has decided that it is appropriate to use a toxicological threshold of 1.5 µg/day as a basis for determining the uniform limit. The threshold has been based on:

- the acceptable exposure levels which have been used in evaluations of flavoring agents by JECFA (Joint FAO/WHO Expert Committee on Food Additives) and in evaluations of indirect additives by the USFDA (Food and Drug Administration), and
- the ADIs (Acceptable Daily Intakes) of chemicals that had been already evaluated by JMPR (Joint FAO/WHO Expert Meeting on Pesticide Residues) or JECFA or in Japan.

The uniform limit has been set at 0.01 ppm so that the estimated intake of agricultural chemicals to which the limit would be applied does not exceed 1.5 µg/day when based on the food consumption of Japanese population. In January 2005 the European Union (EU), which plans to introduce a positive list system, established the uniform level at 0.01 ppm. Considering such circumstances, the MHLW has decided that the limit is reasonable.

For chemicals for which the ADIs set by JMPR or JECFA are extremely low, MRLs have been established at ND (not-detected level), instead of the uniform limits. For substances for which determination limits for analytical methods used in monitoring tests conducted by the Japanese local governments exceeds 0.01 ppm, the corresponding LOD of the analytical methods has been set.

B. Exempted substances

Exempted substances target pesticides, veterinary drugs, and feed additives which are used during the production of crops and aquatic products, and substances which are produced by chemical changes of these agricultural chemicals in food. The selection of exempted substances has been based on the following concepts when these agricultural chemicals themselves and their decomposition products could remain in food as a result of application in food production.

- i. Agricultural chemicals and their decomposition products which are determined not to pose adverse health effects, given residue levels and forms, even if these chemicals remain in crops and animal products, including sea foods, to certain levels.
- ii. Specified agricultural chemicals shown in the Agricultural Chemicals Regulation Law, and chemicals for which registration withholding limits are not established and which are determined not to pose adverse health effects even if crops exposed to these chemicals are consumed.
- iii. Agricultural chemicals which are determined not to require any MRL in foreign countries and whose uses are not restricted.

C. Provisional MRLs

MRLs which had been established before the FSL was amended in May 2003 did not cover all standards, including Codex standards and registration withholding limits for

substances which are permitted for use in Japan. From the viewpoint of protection of public health and smooth implementation of the system, it was necessary to provisionally establish MRLs for chemicals without MRLs. In establishing provisional MRLs, Codex standards and other necessary information have been considered.

Provisional MRLs have been established taking into consideration:

- i. Codex standards,
- ii. Registration withholding limits based on the Agricultural Chemicals Regulation Law, limits of determination for veterinary drugs at the time when they were authorized based on Pharmaceutical Affairs Law (Law No. 145, 1960), or limits of determination for feed additives at the time when they were authorized based on the Law for Safety Assurance and Quality Improvement of Animal Feed (Law No. 35, 1953), and
- iii. Standards established by countries where MRLs are assumed to be established based on toxicity study data equivalent in quality to those used in scientific evaluations by JMPR and JECFA. These countries are Australia, Canada, EU, New Zealand, and United States.

For those chemicals categorized in either of the following two types, ND has been set instead of numerical limits: 1) genotoxic carcinogens and 2) chemicals that have been determined by JMPR or JECFA as those for which the ADI cannot be set. Separately from numerical limits, requirements/restrictions have been imposed on certain types of substances, including antibiotics, antibacterials, substances naturally occurring in foods, and chemicals for which standards are already set for food additive uses, and on applications of MRLs to processed foods.

The proposed provisional MRLs took effect on the date of implementation of the positive list system as compositional standards for food stipulated in Article 11 Paragraph 1 of the FSL. Basically, no change has been made for MRLs already established based on Article 11 Paragraph 1.

<Progress of the activity>

October 2003

The first draft published (draft provisional MRLs only).

August 2004

The second draft published (uniform level, exempted substances, and provisional MRL).

June 2005

The final draft published (uniform level, exempted substances, and provisional MRL).

October 24, 2005

As the result of discussion based on the above concepts, the Pharmaceutical Affairs and Food Sanitation Council reported to the Minister of Health, Labour and Welfare that

- (1) the uniform limit should be established at 0.01 ppm,
- (2) 65 exempted substances should be designated, and

Appendix to Annex 2

(3) provisional MRLs should be established for 758 chemicals.

November 29

Notifications on the positive list system were published in the official gazette *Kanpo*.*

MHLW Notification No. 497 (Uniform limit)

MHLW Notification No. 498 (Exempted substances)

MHLW Notification No. 499 (Provisional MRLs, etc.)

May 29, 2006

The Positive List System took effect.

The MHLW intends, on a systematic basis, to ask the FSC to conduct safety evaluation for agricultural chemicals for which provisional MRLs have been established.

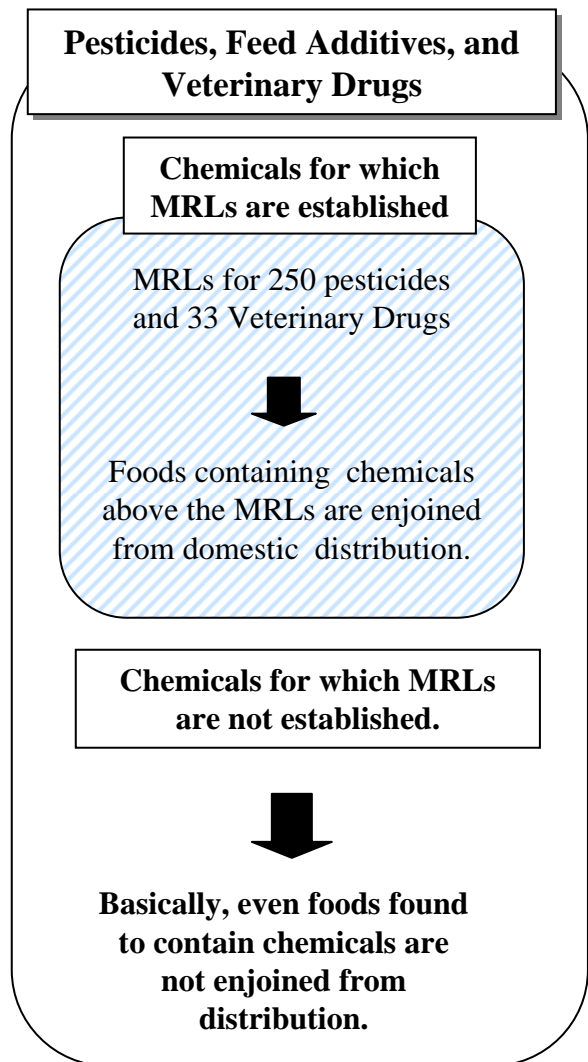
* The uniform limit, exempted substances, and provisional MRLs are accessible in English at:

<http://www.mhlw.go.jp/english/topics/foodsafety/positivelist060228/index.html>

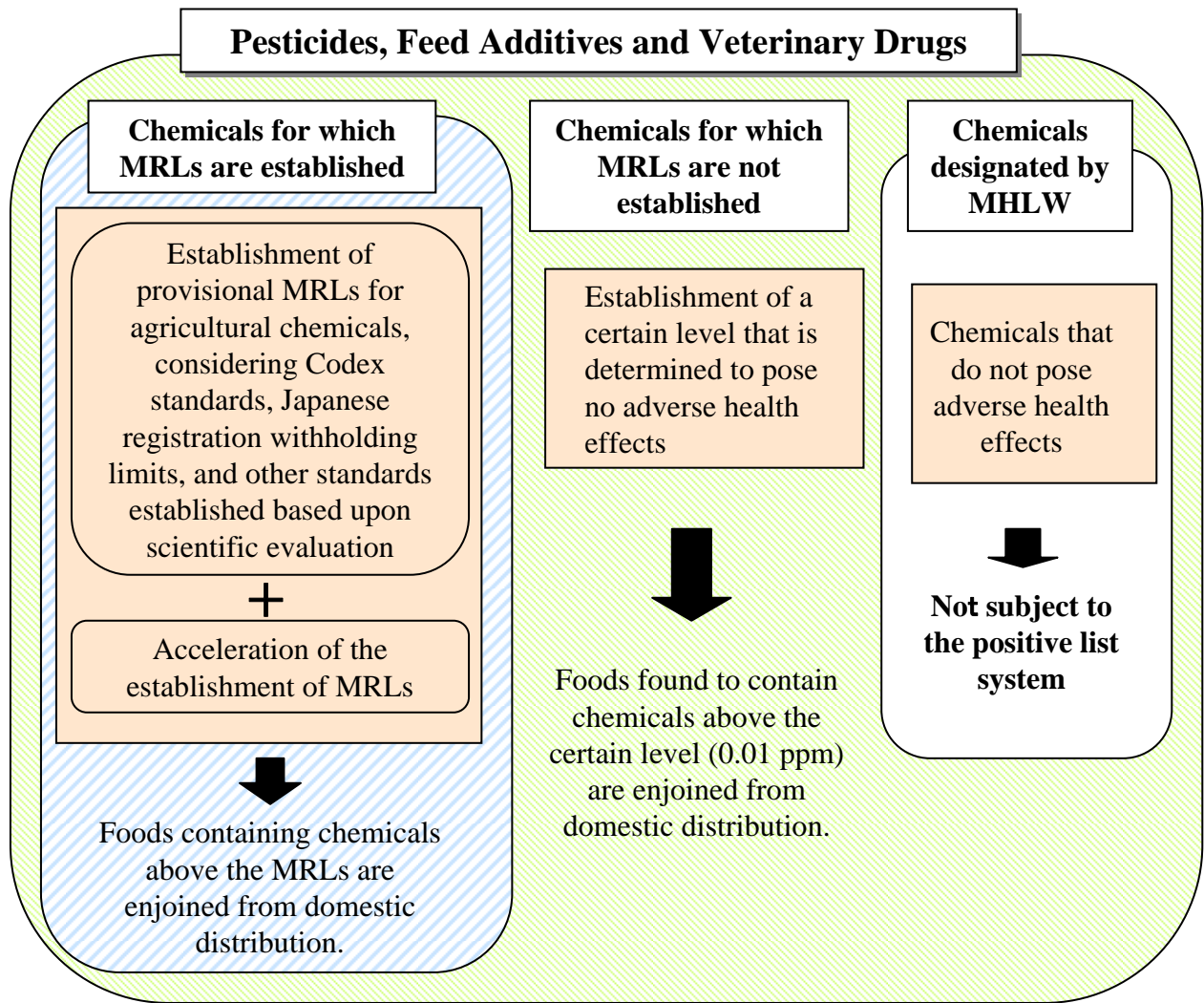
<http://www.ffcr.or.jp/zaidan/FFCRHOME.nsf/pages/MRLs-p>

Positive List System for Agricultural Chemical Residues

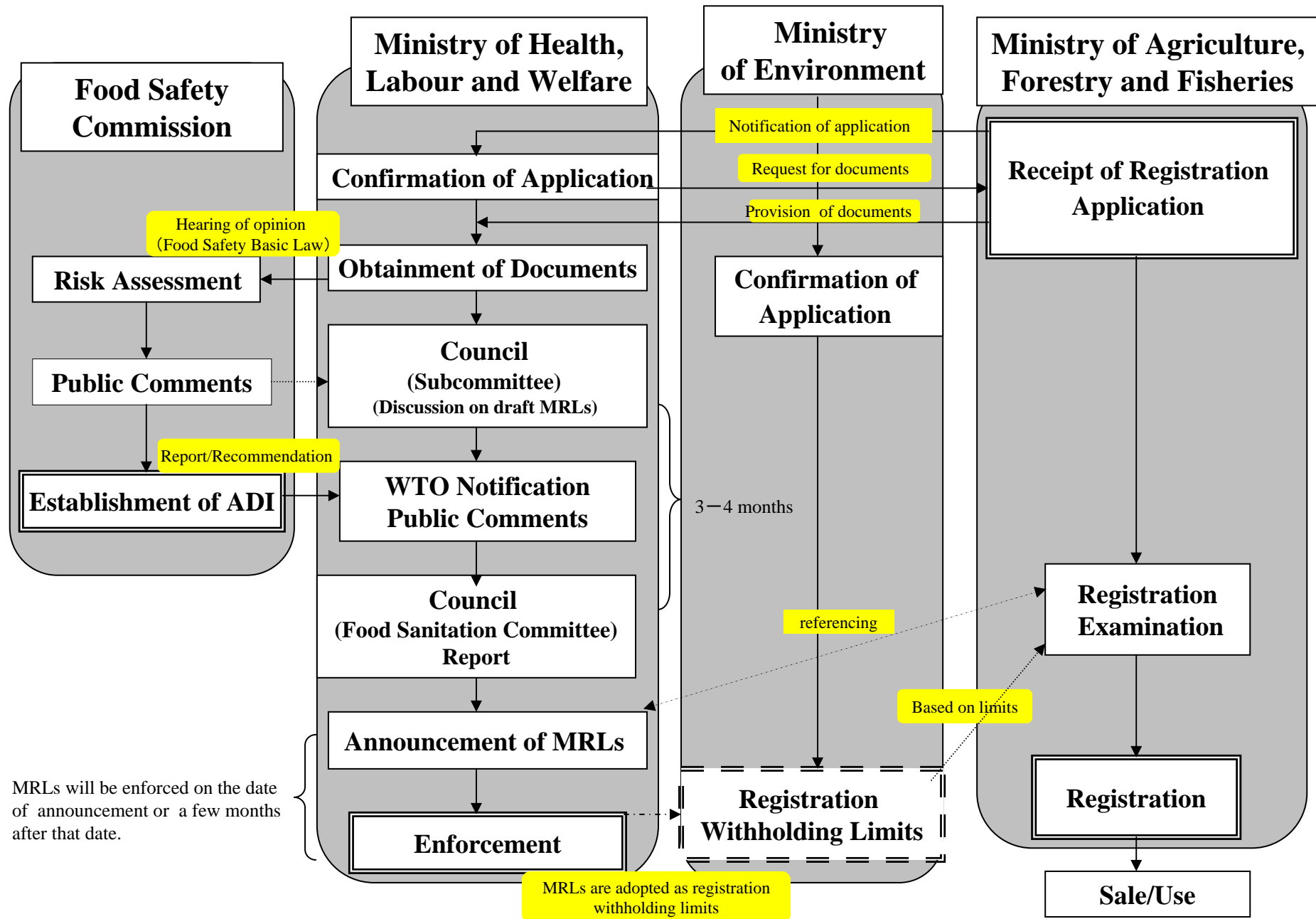
【Before Implementation】



【After Implementation】



Pesticide Registration and Establishment of MRLs



Annex 4.

Basic principles for establishment of maximum residue limits for pesticides in agricultural products

1. The “ADI” and “exposure estimate” are at the core of setting residue standards for pesticides in food (maximum residue limits: MRLs).

- The determination of the ADI¹ is globally based on the following method:
First, a no-observed-adverse effect level (NOAEL) is obtained, based on results of long-term animal safety studies. The NOAEL refers to a level that does not have any adverse effect on the health of the experimental animals. Then, the ADI is calculated by dividing the NOAEL by a safety factor (usually 100) obtained from inter-species variability between humans and test animals and intra-species variability between human individuals.
- In Japan, the expected exposure level of a pesticide is estimated on the basis of the Theoretical Maximum Daily Intake (TMDI) method (TMDI: the sum of all intakes obtained by multiplying MRLs² by the average intake³; see the diagram below) of each target agricultural product and the Estimated Daily Intake (EDI) method.

The setting of MRLs is normally based on the following step:

First, it is evaluated whether the acceptable daily intake (ADI) can be established for a target pesticide, based on the results of safety studies. If the evaluation indicates that an ADI can be established, then draft MRLs for which pesticide are set, based on residue study results, and international standards and other countries' standards.

Second, the expected exposure level⁴ is estimated using draft MRLs.

Third, if the estimated exposure level does not exceed the acceptable intake based on the ADI, the draft MRLs are adopted as national MRLs, because it is determined that this level of consumption of the pesticide will not affect the health of Japanese people. If the estimated exposure level exceeds the acceptable intake, all factors involved in the estimation of pesticide intake are reviewed to correct a possible overestimate. If it is determined that an ADI cannot be established, MRLs are set as “no detection,” or ND for each. In practice, the pesticide is not allowed to remain in

agricultural products.

2. Japan uses a new method for exposure estimation, in which the TMDI method and EDI method are combined. The EDI method was introduced in 2000 to improve a major drawback of the TMDI (an expected exposure level based on the TMDI method is usually an overestimate of the true pesticide intake). For example, the TMDIs of two pesticides (fenitrothion and malathion) out of 246 pesticides having MRLs exceed 80% of the corresponding ADI. However, it is reported that the Market Basket Survey⁵⁾ for these two chemicals found that the estimates of exposure levels for the chemicals fell between 0.1–2.9% of each ADI.

3. The EDI method, published by the WHO (World Health Organization) in 1997, is a more practical method, which is suitable for estimating actual exposures. The EDI method is based on residue test results for pesticides in agricultural products. The United States has already adopted a similar method.

Currently, Codex MRLs established by the Joint FAO/WHO Codex Alimentarius Commission are based on this method. Safety will be confirmed by comparing the ADI with exposure estimates obtained using the method.

4. In the new Japanese method, as long as the exposure estimate obtained based on the new method does not exceed the acceptable intake, international standards are adopted as Japanese MRLs. Otherwise, appropriate action is taken, in light of Japanese dietary patterns, such as the adoption of MRLs stricter than the international standards.

5. The new exposure assessment method is basically similar to the TMDI method for the estimation of the dietary intake of pesticides (a sum of all intakes obtained by multiplying the residue of the target pesticide in each crop by the average consumption of each crop). However, various factors below are considered in estimating residue levels in crops and consumption of crops.

- a. Mean residue levels from supervised trials
- b. Residue in edible portions
- c. Effect of processing and cooking on residue levels
- d. Food consumption data, including subgroups of the population, such as infants and young children
- e. Exposure through pathways other than target crops for MRLs, including

other foods, water, and air

In practice, the exposure estimate of a pesticide from target crops is compared with the acceptable daily intake of the pesticide to confirm that the estimates do not exceed each acceptable intake. This procedure enables the safety assurance of pesticide residues for the entire nation including certain subgroups: infants and young children, pregnant women, and the elderly. Both exposure estimates and acceptable intakes are obtained, as given below, separately for the entire nation and for the three subgroups.

$$\begin{array}{l}
 \boxed{\text{Exposure}} = \boxed{\text{Residue level of crop A}^6} \times \boxed{\text{Intake of crop A}^7} + \\
 \boxed{\text{Residue level of crop B}} \times \boxed{\text{Intake of crop B}} + \\
 \dots \dots \dots + \\
 \text{(Exposure = Sum of each intake of a pesticide)}
 \end{array}$$

$$\boxed{\text{Acceptable intake from crops}} = \boxed{\text{ADI mg/kg of body weight}} \times \boxed{\text{Average body weight}^8} \times \boxed{\text{Factor}^9 \text{ based on exposure from other pathways, such as water}}$$

Outline of the new exposure assessment method

First step

To compare the TMDI with the acceptable intake of a pesticide for four groups: the entire nation and three subgroups (infants and young children, pregnant women, and the elderly). The acceptable intake is set, taking into account exposure from other pathways such as water and air.

If the TMDI is less than the acceptable intake for each of the four groups, the draft MRLs are adopted. In this case, the second step is not taken, because the safety of the pesticide residues is considered to be secured. If the TMDI exceeds the acceptable

intake for one of the four groups, assessment proceeds to the second step.

Second step

To use refined exposure estimates based on the Japanese EDI method for comparing with each acceptable intake. Comparison is conducted separately for each estimate obtained for the entire nation and three subgroups (infants and young children, pregnant women, and the elderly).

If the Japanese EDI (estimated daily intake) is less than the acceptable intake for each of the four groups, the adopt draft MRLs are adopted because the safety of pesticide residues is considered to be secured. If the EDI exceeds the acceptable intake for one of the four groups, assessment proceeds to the third step.

Third step

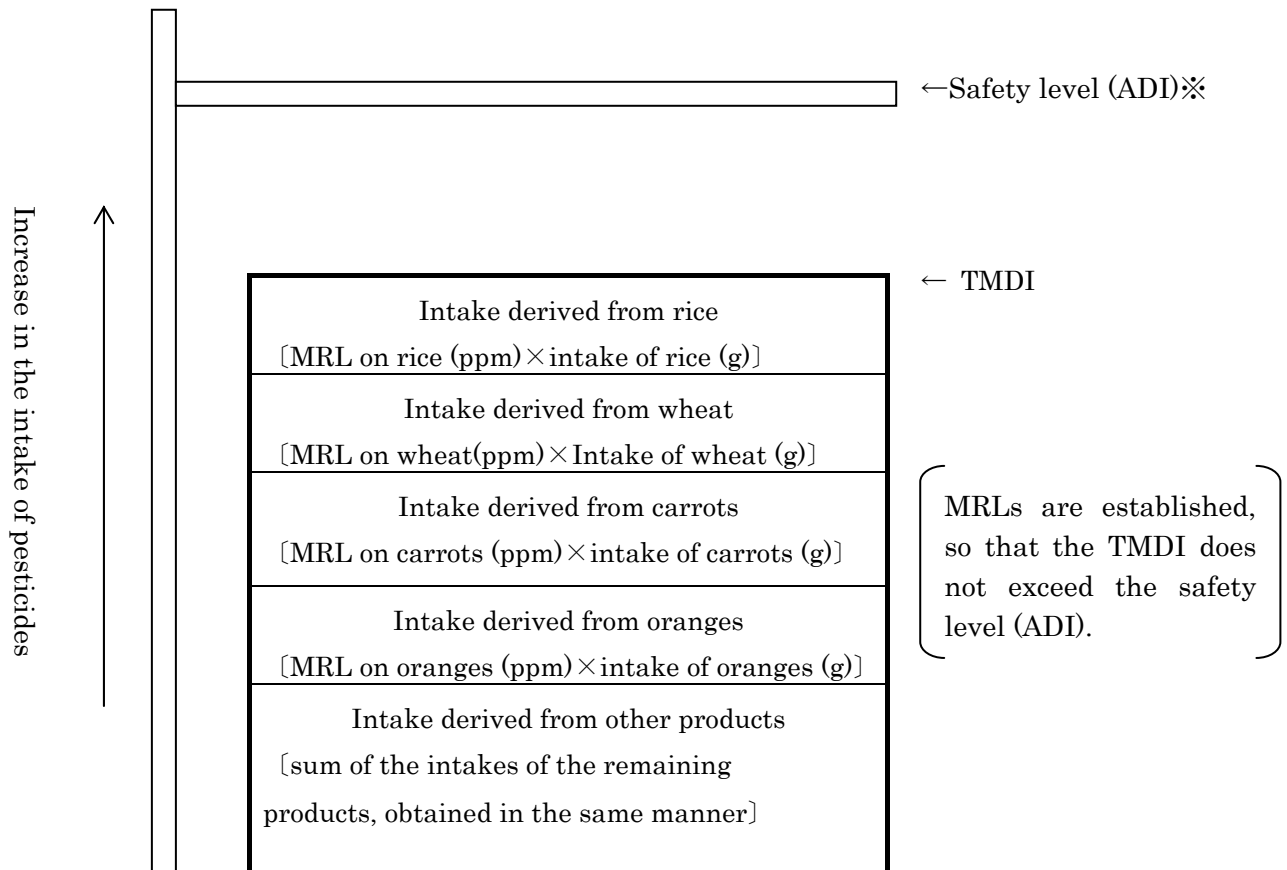
Appropriate measures, such as adoption of stricter MRLs are taken, because the adoption of the draft MRLs could give rise to adverse effects on the protection of public health.

Note:

1. “Acceptable Daily Intake” (ADI) refers to the estimate of the amount of a substance that can be ingested daily over a lifetime without appreciable health risk to the consumer. It is normally expressed in milligrams of the substance per kilogram of body weight.
2. “Average intake” refers to the amount of a food consumed per person per day, obtained from the National Nutrition Survey (food intake survey).
3. Draft MRLs are established based on international standards and residual levels of a target pesticide in crops obtained from field tests.
4. “Expected exposure level of a target pesticide” refers to the amount of a pesticide received by consuming crops that were treated with the pesticide.
5. “Market Basket Survey” refers to a survey to identify actual intakes of pesticides from crops in the marketplace, based on data from the National Nutrition Survey (food intake survey). Chemical analyses are conducted after samples are prepared/cooked as they would be normally.

6. As a residue level, use the amount of pesticide residues, based on residue tests for crops, residue data for edible portions, and the effects of cooking and processing on residue levels.
7. As the intake of a target crop, use the consumption of each crop for the whole population (per capita) and three subgroups (infants and young children, pregnant women, and the elderly) separately, based on data from the National Nutrition Survey .
8. As a mean body weight, use the mean of body weights of the people surveyed for the whole population and the three subgroups (infants and young children, pregnant women, and the elderly) separately, based on data from the National Nutrition Survey.
9. The factor is based on exposure to pesticides only from crops by deducting exposure from pathways other than target crops, such as other foods, water, and air. Usually, 0.8 (80%) is used.

Diagram: TMDI method



* In order to determine the acceptance daily intake (ADI) of each pesticide, first a certain amount (maximum no observed adverse effect level), at which the pesticide administered does not induce any effect on experimental animals, is obtained on the basis of animal experiments. Then, the amount is multiplied by a safety factor. This is to provide an adequate safety margin. The order of 100 as safety margin is widely used.