Japan MRL Procedures

Global Minor Use Summit
3-7/December/2007
FAO Headquarters, Rome, Italy
Food Safety Approach in Japan
Food Safety Basic Law  Enforced in July 2003

- Principles on Food Safety Administration
- Establishment of Food Safety Commission
- Responsibilities of Government, Food Producers and Consumers
- Application of Risk Analysis in Food Safety Administration
**MEASURES FOR “FOOD SAFETY”**

**RISK ASSESSMENT**

- Food Safety Commission

  - To conduct a risk assessment.
  - To recommend that agencies in charge of risk management implement necessary measures for food safety, based on the risk assessment results.
  - To monitor the risk management by related agencies.
  - To collect and analyze domestic and international information on food safety hazards.
  - To comprehensively manage total risk communication including activities of the risk management agencies.

**RISK COMMUNICATION**

- Disclosure of information on food safety
- Securing consumers’ opportunities to express their opinions

**RISK MANAGEMENT**

- **MHLW**
  - Quarantine Stations
  - Regional Bureaus of Health and Welfare
  - Health Centers, etc.

- **MAFF**
  - Agricultural Administration Offices
  - Food and Agricultural Materials Inspection Center (FAMIC), etc.

**Food Safety Basic Law**

**Food Sanitation Law, etc.**

**Agricultural Chemicals Regulation Law, etc.**
Relationship between the registration of pesticides and the regulations on pesticide residues in foods

The Agricultural Chemicals Regulation Law (ACRL),
The Ministry of Agriculture, Forestry and Fisheries (MAFF)
The Ministry of the Environment (MOE)

The Food Sanitation Law (FSL),
The Ministry of Health, Labor and Welfare (MHLW)

The Food Safety Basic Law (FSBL),
The Cabinet Office
Agricultural Chemicals Regulation Law

**Purpose**

The ultimate purposes of the law are to make agricultural production stable and to prevent any adverse effect to human health and the environment caused by pesticide use. This is done through a registration system.

**Two ministries are mainly involved:**

1. **Ministry of Agriculture, Forestry and Fisheries/ACIS**
   
   Examination based on criteria (i.e. "the registration Withholding Standards") false description in application, damage to crops, damage to users, designation misunderstanding efficacy, inferior efficacy, inconformity with official standards, persistency in crops, persistency in soil, water pollution and damage to aquatic animals and plants

2. **Ministry of the Environment**
   
   Establishment of the Standard on persistency in soil, damage to aquatic animals and plants, water pollution and **persistency in crops**
   
   MRLs (Food Sanitation Law) are used as this standard.
Pesticide Registration Scheme

**Risk Management**

- **Ministry of AFF**
  - Plant Products Safety Division, Food Safety and Consumer affairs Bureau
  - **Receipt of registration-application form**
  - **Registration**
  - **Establishment of Official Standard**
  - **Designation of Low risk pesticide**
  - **Establishment of standard for withholding registration except the standard established by Ministry of Environment**

**Risk Evaluation**

- **Ministry of Health Labor and Welfare**
  - Designation of poisonous and deleterious substances
  - Establishment of MRLs on pesticides residue

- **Ministry of Environment**
  - Establishment of the withholding standard regarding human health and environmental safety

- **Cabinet Office**
  - Food Safety Commission
  - Establishment of ADI

- **Central Environmental Council**

- **Agricultural Materials Council**

**FAMIC**

Agricultural Chemicals Inspection station (ACIS)

- **Examine registration application form etc.**
- **Evaluation of the data etc. (See below)**

- ○ Safety to human health and livestock etc.
- ○ Impact to soil, water and air environment
- ○ Safety of impurities of technical grade of Active Ingredient (TGAI)
- ○ Physical/Chemical properties of Active Ingredient and end-use product
- ○ Efficacy and phytotoxicity
- ○ Residue in crops
- ○ Impact to non-target organisms

**Application via ACIS**

- Manufacturer or Importer

- **Grant the Registration Card**

- **Manufacturing Processing or Import of Pesticide**

ACIS is one of Departments of Food and Agricultural Materials Inspection Center (FAMIC). It is an Incorporated Administrative Agency under MAFF.
Food Sanitation Law

Purpose

This law aims to prevent the occurrence of health hazards arising from eating and drinking by implementing regulations and other necessary measures from the standpoint of public health to ensure food safety, so as to protect the public health.

The law is roughly divided into two parts:

(1) establishment of standards including specification and standards for food, standards for facilities, standards for management/operation, and standards for labeling;

(2) inspections and guidance including inspection by national government at import and inspections and guidance by local and municipal governments for domestic food businesses.
Positive List System for Pesticide Residue in Food
Summary of the Positive List System for Agricultural Chemical Residue in Food

- Residues in foods resulting from the use of Veterinary Drugs, Feed Additives and Pesticides

Food in which residue of agricultural chemical exceeds a certain level, “Default Level”, shall not be marketed.

  But the case that the MRL for the residue is established and the residue level does not exceed the MRL is exclusive.

- The regulation applies to domestic and import foods.

- The regulation has been enforced since 29 May 2006.
Pesticides, Feed Additives, and Veterinary Drugs

Chemicals for which MRLs are established

MRLs for 250 pesticides and 33 Veterinary Drugs

Foods containing chemicals above the MRLs are enjoined from domestic distribution.

Chemicals for which MRLs are not established.

Basically, even foods found to contain chemicals are not enjoined from distribution.
Pesticides, Feed Additives and Veterinary Drugs

Chemicals for which MRLs are established

Establishment of provisional MRLs for agricultural chemicals, considering Codex standards, Japanese registration withholding standards, and other standards established based upon scientific evaluation

Acceleration of the establishment of MRLs

Foods containing chemicals above the MRLs are enjoined from domestic distribution.

Chemicals for which MRLs are not established

Establishment of a certain level that is determined to pose no adverse health effects

Foods found to contain chemicals above the certain level (0.01 ppm) are enjoined from domestic distribution.

Chemicals designated by MHLW

Chemicals that do not pose adverse health effects

No subject to the positive list system

Enforcement of Positive List System since May 2006
Government Notifications on 29 November 2005 related to the Positive List System

- No. 497 Default Level 0.01 ppm is established as the default level.

- No. 498 Substances exempted from the system 65 substances are listed.

- No. 499 Provisional MRLs (for 758 substances) and other provisions for the system are established.
Establishment of the Provisional MRLs

① Codex standards (International standards)

② Registration Withholding Limits and Limit of determination of Veterinary Medicine

③ Standards in foreign countries that have been based upon scientific toxicity evaluations required by JMPR (the Joint FAO/WHO Meetings on Pesticide Residues) and JECFA (the Joint FAO/WHO Expert Committee on Food Additives).
  (Australia, Canada, New Zealand, USA, and European Union)

Legal Status of provisional MRLs

The provisional MRLs are applied as the legal standards based on Article 11 of the Food Sanitation Law.
Establishment of maximum residue limits for pesticides

**Toxicity assessment**
- Evaluation based on various types of animal test
- Setting of no observed adverse effect level (NOAEL)
- Establishment of Acceptable Daily Intake (ADI)

**Residue study results**
- Codex standards
- Consideration of proposed MRL

**Exposure assessment**
- Theoretical Maximum Daily Intake (TMDI) method
- Estimated Daily Intake (EDI) method
- Comparison of acceptable intake
- with estimated exposure

Validation of proposed MRL

Establishment of MRL
Risk Assessment by FSC

Data to be evaluated

Animal metabolism          Skin sensitization
Plant metabolism           Subchronic toxicity
Fate in soil/water         Chronic toxicity/carcinogenicity
Photolytic fate in water   Reproductive/developmental toxicity
Residue in crops/soil      Genotoxicity
Acute Toxicity             General pharmacology
Skin and eye irritation    Others

The evaluation result is disclosed to the public as the evaluation report.
# Estimation of Daily Intake

Example of Theoretical Maximum Daily Intake (TMDI) estimation

**Name:** AAAA

<table>
<thead>
<tr>
<th>Food</th>
<th>Proposed MRL (mg/kg)</th>
<th>Entire nation</th>
<th>Infant (1 to 6 years old)</th>
<th>Pregnant women</th>
<th>Elderly (65 years old or over)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ff</td>
<td>Intake</td>
<td>ff</td>
<td>Intake</td>
<td>ff</td>
</tr>
<tr>
<td>Corn</td>
<td>0.05</td>
<td>2.5</td>
<td>0.13</td>
<td>4.3</td>
<td>0.22</td>
</tr>
<tr>
<td>Beans, dry</td>
<td>0.5</td>
<td>1.4</td>
<td>0.70</td>
<td>0.5</td>
<td>0.25</td>
</tr>
<tr>
<td>Cabbage</td>
<td>2</td>
<td>22.8</td>
<td>45.60</td>
<td>9.8</td>
<td>19.60</td>
</tr>
<tr>
<td>Tomato</td>
<td>0.5</td>
<td>24.3</td>
<td>12.15</td>
<td>16.9</td>
<td>8.45</td>
</tr>
<tr>
<td>Egg plant</td>
<td>0.5</td>
<td>4.0</td>
<td>2.00</td>
<td>0.9</td>
<td>0.45</td>
</tr>
<tr>
<td>Lettuce</td>
<td>2</td>
<td>6.1</td>
<td>12.20</td>
<td>2.5</td>
<td>5.00</td>
</tr>
<tr>
<td>Cherry</td>
<td>**</td>
<td>**</td>
<td>***</td>
<td>**</td>
<td>***</td>
</tr>
<tr>
<td>Strawberry</td>
<td>0.5</td>
<td>0.1</td>
<td>0.10</td>
<td>0.1</td>
<td>0.10</td>
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<tr>
<td>Grape</td>
<td>3</td>
<td>5.8</td>
<td>17.40</td>
<td>4.4</td>
<td>13.20</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADI%</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**ff:** Food factor

Average body weight: 53.3kg(entire nation), 15.8kg(infant), 55.6kg(pregnancy), 54.2kg(elderly)
Application of Import Tolerance
A Guideline for “Import Tolerance”

A Guideline on application for establishment and revision of the Japanese MRL for the residues of agricultural chemicals used outside Japan

Notification No. 0205001, 5th February 2004
from Director-General, Department of Food Safety, MHLW

Further information:
http://www.mhlw.go.jp/english/topics/foodsafety/dl/importguideline.pdf
Application of Import MRL

“Any person may apply to the Minister of Health, Labour and Welfare for establishment or revision of MRLs for an agricultural chemical in the case that the chemical is approved in a country for foods exported to Japan.”

“If applicant is abroad, an appropriate contact person in Japan should be identified to handle the application.”
Other Requirements

Submission of the following documents are recommended.

- Information on registration of the substances in other countries
- Proposal of MRL to be established
- Analytical method for the residue in food
- Processing data if available
- Revocation or other changes of registration of the chemical
Data Requirements for the Application

“A set of toxicity data and residue date give in the “Data Requirements for Supporting Registration of Pesticides” - Director-General, Agricultural Production Bureau, MAFF, Notification No.12-Nousan-8147, 24 November 2000 - (excluding effects of aquatic animals and plants, effects on beneficial creatures other than aquatic animals and plants, and study data on water contamination )”

“The study results and related documents given in the guideline can be replaced by other documents sufficient to conduct evaluation for establishment and revision of MRLs.”

Information on data requirements;
http://www.acis.famic.go.jp/eng/shinsei/index.htm
GLP Compliance

“In principle, studies should comply with the GLP requirements.”

Language

“The executive summary should be written in Japanese. Other accompanying documents such as study reports may be written in English.”
A Guideline on application for establishment and revision of the Japanese MRL for the residues of agricultural chemicals used outside Japan Notification No. 0205001, 5th February 2004 from Director-General, Department of Food Safety, MHLW
MHLW FOOD SAFETY INFORMATION

<JAPANESE version>
http://www.mhlw.go.jp/topics/bukyoku/iyaku/syoku-anzen/index.html

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