【S-17】

Development of National Risk Assessment System in Food

Hyo-Min Lee

Division of Risk Assessment Research
National Institute of Toxicological Research
Korea Food & Drug Administration

The included newly revised food sanitation law was announced at July 28, 2007 and the article 13 in the revised law described that risk assessment should be undertaken in the case to be suspected that the food, equipment & packaging material may present a risk to health due to its hazardous substances. Enforcement Decree of the Food Sanitation Law, Article 2-2 described four primary steps in the process of risk assessment, i.e., hazard identification, exposure assessment, hazard characterization, and risk characterization.

The establishment of national risk assessment system in food is intended to prepare for changing of circumstances under the basis of the WTO/DDA declaration and to harmonize SPS (Sanitary and Phytosanitary) measures on international standards as contracting part in CODEX and other relevant international organization. No national regulatory system is exactly same as others. Although their purposes are largely the same and their officials share a similar public health viewpoint, health regulatory agencies in different nations often see issues differently. Food safety standards are the measures of compliance regulations enacted by the government to protect the health and safety of our citizens and the environment in which we live.

The risk assessment should be based on a sound science with working rationale and national policy should be established in process of risk assessment. Moreover, risk management as the process of weighing policy alternatives based on results of risk assessment. A typical example is whether the approach of threshold and non-threshold can be differently applied. Also, research to improve risk assessment methodology and develop managing strategy needed in regulatory region should be implemented under the governmental support.

Development of National Risk Assessment System in Food

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Background

Introduction of Risk Assessment System in Domestic Food Management

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- For a positive confrontation on changing of circumstances under the basis of the Doha declaration and entrance in WTO(World Trade Organization) system.
- For a establishment of national risk assessment system to harmonize SPS(Sanitary and Phytosanitary Measures) measures on international standards, guidelines and recommendations and as contracting part in CODEX and other relevant international organization.

Introduction of Risk Assessment System in Domestic Food Management

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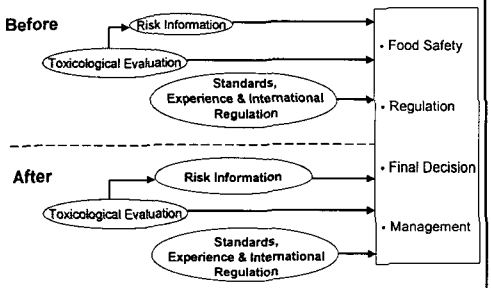

Risk Assessment Procedure suggested in Revised Food Sanitation Law

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Hazardous Substances

Chemical Factor

Pesticides, Heavy Metals, Food Additives, Animal Drugs, Environmental Contaminants and Hazardous Reaction Products in Food Processing et al.

Physical Factor

External Form of Foods and Foreign Substances et al.

Microbial Factor

Food-born Pathogen et al.

Enforcement Decree of The Food Sanitation Law Article 2-2

Subject

Foods

Equipment, Packaging Materials

Risk Assessment

Revised The Food Sanitation Law

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Article 13 (Risk Assessment)

.....

Risk Assessment should be undertaken in case to be suspected that a food equipment & packaging material may present a risk to health due to hazardous substances related with Article 4 or Article 8 .....

→ Article 4 (Ban of a food may present a risk to health)

.....

2. Food contaminated by hazardous substances or toxicants was confirmed and to be suspected.....

→ Article 8 (Ban of tainted equipment and packaging materials)

Equipment and packaging materials contaminated by hazardous substances or toxicants were confirmed and to be suspected.....

Enforcement Decree of The Food Sanitation Law

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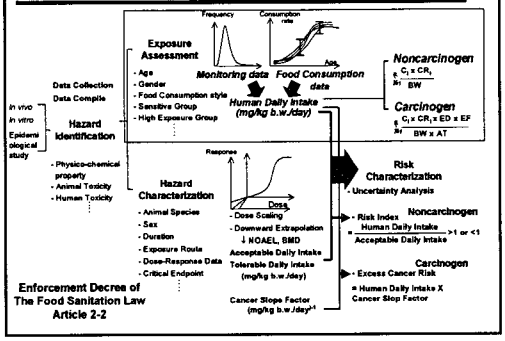
Article 2-2

1. Subjects of Risk Assessment

- Food was prohibited the trade on the internal market by international agency such as CODEX and foreign government due to apprehension of a risk to health.
- Food contaminated by hazardous substances or toxicants was confirmed and to be suspected in the internal institutions or internationally.
- Food recognized by Food Sanitation Council to be suspected that may present a risk to health through request of risk assessment by Consumer Organizations or Korean Society of Food Science & Technology based on 「The Consumer Protection Law」 Article 19.
- Food produced by genetically modified technique and using new ingredient that safety was not built up.

Process of Risk Assessment & Flowchart of Related Data



Implementation of Risk Assessment based on Toxicity Data and Monitoring Data

Hazard Identification ⇨ Exposure Assessment ⇨ Hazard Characterization ⇨ Risk Characterization

Factor having Toxicity Data with Monitoring Data ⟹

Factor having Monitoring Data with Toxicity Data ⟹

Factor without Monitoring Methodology ⟹

Enforcement Decree of The Food Sanitation Law Article 2-2

Dependent Rate	Toxicity Data	Monitoring Data
National Data (made in)	10% ↓	95% ↑
Foreign Data (made in)	90% ↑	5% ↓

Early History

Regulatory Applications of Quantitative Risk Assessment of Chemical Carcinogens

- **Arnold Lehman** (Chief toxicologist at the FDA in 1940-1960)

⇒ stated in an article in 1949 that carcinogenic food additives would not be permitted.

- **Druckrey** (1943), **Berenblum** (1945)

⇒ showed that exposure to small persistent doses of carcinogens could be more effective than single large doses in producing tumors.

- **Shubic** (1950)

⇒ discovered that a single exposure to a carcinogenic "initiator" could produce a latent effect that was essentially permanent and that could be manifested later even if treatment with the "promoter" were delayed for up to half the lifetime of the animal.

For carcinogens ⇒ The importance of low doses and continuous exposure

Early History

Regulatory Applications of Quantitative Risk Assessment of Chemical Carcinogens

- **U.S Department of Health, Education and Welfare(HEW), 1971**

; For carcinogenic agents a safe level for man cannot be established by application of our present knowledge. The concept of **" acceptable levels of risk"** represents a more realistic notion.

⇒ Suggestion of the induction of a virtually safe level for a carcinogen by downward extrapolation from observed animal data(Mantel and Bryan, 1961)

1. Testing should be done at high dose and under experimental conditions likely to yield maximum tumor incidence.
2. At least two species should be used for all carcinogenicity studies
3. For compounds judged carcinogenic at test levels, a virtually safe dose could, in principle, be estimated by downward extrapolation using some arbitrarily selected but conservative dose-response curve.

Early History

Regulatory Applications of Quantitative Risk Assessment of Chemical Carcinogens

- By the early 1970s, regulators at the FDA and EPA accepted the concept of acceptable cancer risk and the necessity for dose extrapolation to determine an upper bound to that risk.

- **Gebring and Blau, 1977**

; Large doses could exceed metabolic and physiological thresholds, leading to prolonged retention in the body and disproportionate increases in carcinogenic electrofiles

⇒ There are several examples of food substances that are carcinogenic at high dosed but are probably not carcinogenic at lower doses.

; Saccharin, ortho-phenylphenate, sulfamethazine, formaldehyde, butylated hydroxyanisole and d-limonene.

- **National Research Council, 1993**

; The NRC Committee on Risk Assessment Methodology(CRAM) recommened the continued use of the MTD and did not reach agreement on how the additional information on mechanisms of carcinogenicity should be used (without producing a satisfactory alternative)

In the USA

Regulatory Applications of Quantitative Risk Assessment(QRA)

- Food additives that are found to be carcinogenic in animal feeding studies are not approvable; Substances found to be carcinogenic in rodent cancer bioassays, like saccharin and cyclamate, are therefore illegal in the USA.

Exception ⇒ QRA may be used to set acceptable levels of exposure; animal drugs and feed additives may be permitted if the extrapolated risk is less than in 1,000,000(1×10^{-6}) (US FDA, 1985)

Exception ⇒ Unavoidable food contaminants such as aflatoxins, discontinued pesticide such as DDT, and environmental contaminations such as dioxins, polynuclear hydrocarbons and nitrosamines, are also permitted in food.

Comparison with Other National Regulatory Systems

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Although their purposes are largely the same and their officials share a similar public health viewpoint, health regulatory agencies in different nations often see issues differently.

No one national regulatory system is exactly like other

- National Laws
- National Cultures
- National Experiences
- National Interests

- Different Attitude
- Different Procedure
- Different Regulation

Some Rationale and Policy should be established in National Regulatory System

(Risk Assessment & Risk Management)

Comparison with Other National Regulatory Systems

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1. QRA of carcinogens;
   The USA stands virtually alone in its major reliance on QRA

   Two basic reasons for the FDA's use of QRA
   1) Prohibits adding any carcinogen to food
   2) The animal bioassay is scientifically relevant to the human response

2. Ban or Permission;

- The USA which bans cyclamates, whereas these are permitted food additives in Canada and many EU countries.
- The EU banned the use of anabolic steroids in livestock production. Despite the fact that the WHO Joint Expert Committee on Food Additives found that the use of the hormone was safe, the EU nevertheless prohibited such use on the alleged grounds of consumer preference.
- This is in contrast to the regulation in the USA, where the allowed use of animal hormones in livestock productions is based on scientific determinations that hormones are safe when used as intended.

Comparison with Other National Regulatory Systems

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Tolerable Daily Intake for Dioxins
(TDI, PTWI, PTMI)

- TDI Tolerable Daily Intake
- PTWI Provisional Tolerable Weekly Intake
- PTMI Provisional Tolerable Monthly Intake

	Daily (pg-TEQ/kg/day)	Weekly (pg-TEQ/kg/week)	Monthly (pg-TEQ/kg/month)
WHO(1998)	1 - 4		
EC SCF (May, 2001)		14	
JECFA (June, 2001)			70
Korea(2000)	4		
Japan(1999)	4		
UK FSA (Oct, 2001)	2		

- EC SCF (Scientific Committee on Foods)
- JECFA (The Joint FAO/WHO Expert Committee on Food Additives)
- UK FSA (Food Standards Agency)

Risk Analysis

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; The process consisting of three components: risk assessment, risk management, and risk communication

Framework

The process of weighing policy alternatives in light of results or risk assessment, and, if required, selecting and implementing appropriate control options, including regulatory measures.

The scientific evaluation of known or potential adverse health effects resulting from human exposure to hazards. The process consists of the following steps ; hazard identification, exposure assessment, hazard characterization (dose-response), and risk characterization.

The interactive exchange of information and opinions concerning risk and risk management among risk assessors, managers, consumers, industry, and other interested parties.

Recommendation of the CFSAN Risk Analysis Working Group

NiTR

Risk analysis is a powerful tool that should be used to enhance the scientific basis of regulatory decisions. It should be conducted within CFSAN through the efforts of risk assessment, risk management, and risk communication **teams**.

Risk assessment should be conducted in an iterative manner that allows refinement of the risk assessment question(s), key assumptions, and data used in the model.

The exchange of information(**communication**) within and between the risk analysis teams, with other agencies, and stakeholders(including industry, consumer groups, and other interested parties) should be encouraged by **active participation** in the process and collaboration, when appropriate.

Recommendation of the CFSAN Risk Analysis Working Group

NiTR

To support and promote the use of a risk analysis framework for initiating and conducting ' major' risk assessment, CFSAN should;

1. **Adopt a decision-based approach to identify and select risk assessments** conducted by CFSAN, particularly those that are 'major'(complex and impact or involve multiple offices). Available resources, regulatory needs, and public health concerns should be considered in the selection of risk assessments. This approach should be implemented for microbial risk assessments now, and later expanded to include chemical and other non-microbial hazards.
2. **Establish a procedure** for the conduct of risk assessment within a risk analysis framework. The procedure should identify the boundaries and responsibilities of key participants in the risk analysis process.
3. **Develop criteria to evaluate the quality of data** used for risk assessments and specify what information is needed to scientifically evaluate the usefulness of a study or data set used for risk assessment.
4. **Develop guidelines to evaluate** risk assessments and supporting data developed by stakeholders and submitted to the Center.
5. **Formalize a peer review process** that will encourage critical review and evaluation of CFSAN's risk assessments by government and non-government experts in a manner that improves the science and acceptance of complex risk assessments.
6. **Build capacity** to conduct complex risk assessments by providing training opportunities for current staff, hiring new staff or using contractors(as needed), and acquiring additional resources such as computers, software, and dedicated workspace.

Perspective & Suggestions

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- Detailed rational & policy should be established for the risk assessment and risk management system.
  - Differentiation of risk assessment strategy for carcinogen and noncarcinogen (Threshold or Nonthreshold)
  - Development of applying process in regulatory system based on judgment of carcinogenic agents
    (IARC* & US EPA Classification / US NTP** Report / Other Results)
  - Application of available data & national factors
    (Monitoring Data / Food Consumption Data / Other Exposure Factor)

* International Agency for Research on Cancer
** National Toxicology Program

Perspective & Suggestions

NiTR

- Research to improve risk assessment methodology and develop managing strategy needed in regulatory region applying risk assessment result should be implemented under the governmental support
  - Development the scientific foundation of human health risk assessment
    (Low dose impact, Dose-response assessment using biomarker, Health impact of susceptible group & highly exposed subpopulation, Exposure study in given population, Exposure to Dose Research using PBPK/TK study...)
  - Development and research for good risk management & risk communication
    (Cost-benefit analysis research on some dominant factors related with risk reduction...)