

Food Safety

Official Journal of Food Safety Commission



Food Safety Journal

<https://www.jstage.jst.go.jp/browse/foodsafetyfscj>



Food Safety Commission of Japan

<http://www.fsc.go.jp/english/index.html>

From Editor-in-Chief

Since ancient times, enormous efforts have been devoted to supplying sufficient foods, providing safe foods, and preventing food-borne illnesses. In recent years, such efforts have been directed particularly toward improvement of food supply through innovation and development of agricultural chemicals and food additives, food manufacturing and processing techniques, and food distribution systems. In parallel with the development of science and technology related to the food supply, systems and methods for securing food safety have also progressed markedly in the past decades.

Nevertheless, recent changes in the environment and circumstances surrounding the food supply have continuously raised concerns about food safety. Global warming is anticipated to cause environmental changes, accompanied by changes in distribution of pathogenic and toxigenic microorganisms, and impairment of crop, livestock and fisheries yields, consequently to cause an increase in health risks through more frequent intake of marine toxins, mycotoxins, food-borne pathogens and other hazardous agents. The growth and expansion of the trade and distribution of food, including industrially produced and processed foods, are anticipated to cause large outbreaks of food poisoning and food-borne infections. Novel foods and foods produced by newly developed techniques may also raise concerns for food safety. In view of this situation surrounding the food supply, it is more important than ever to develop the science and technology that focuses on food safety.

Science and technology for food safety involve a large number of research fields of different disciplines, and the research outcomes have been disseminated over a wide range of scientific journals devoted to microbiology, biochemistry, toxicology, and epidemiology, and also agricultural, environmental, and public health science. However, to achieve further development of science and technology for food safety, it is necessary to construct a data and knowledge bank in which research outcomes are gathered and available for anyone requiring them. Taking into account the need for such a bank, we have decided to launch a peer-reviewed open-access electronic online journal in English named *Food Safety - The Official Journal of the Food Safety Commission of Japan*.

The journal publishes original articles, short communications, and reviews covering broad areas of food safety related to the risk assessment of foods as well as risk assessments conducted by the Food Safety Commission of Japan. Papers dealing with the following areas are particularly welcome: (1) pathogenicity or toxicity of biological, physical, and chemical agents concerning food safety; (2) occurrence of biological, physical, and chemical agents in the food chain with emphasis on food safety; (3) epidemiology or control of food-borne illnesses; and (4) safety evaluation of novel foods, including, among many others, nano-materials and genetically modified organisms. We hope that this new journal will be successful in improving the levels of science and technology for food safety, and that it will contribute to the growth of an integrated research field specifically focusing on food safety.

Susumu Kumagai

Editor-in-Chief

Carcinogenicity Assessment for Risk Factors in Food:

Current Issues and a Proposal

Akiyoshi Nishikawa

Biological Safety Research Center, National Institute of Health Sciences, 1-18-1 Kamiyoga, Setagaya-ku, Tokyo 158-8501

In the current carcinogenicity assessment, the threshold is a major issue for genotoxic carcinogens. Carcinogenicity is usually assessed in combination with genotoxicity data. The current assessment methodology is based on the hypothesis that non-genotoxic carcinogens have thresholds but genotoxic carcinogens do not. However, it remains unclear in most cases as to how much the detected genotoxic potential is actually associated with the carcinogenicity at an organ level. To clarify this critical issue, *in vivo* genotoxicity has been investigated in transgenic rodents carrying reporter genes, which can simultaneously detect both genotoxicity and carcinogenicity on each organ basis. Studies of a number of genotoxic carcinogens have revealed good correlations between *in vivo* genotoxicity and carcinogenicity. However, some discordant results have been also found in some cases. Besides experimentally observed values of genotoxicity, MOA or statistics might be taken into account for biological or practical threshold. Then, statistical or mathematical evaluation can provide values of BMDL or MOE even for strictly defined genotoxic carcinogens. Another major issue is concerning extrapolation of animal data for human risk. For this purpose, WOE approaches based on MOA may be extremely useful. Experiments using transgenic rodents such as *p53*, *nr12* or CAR knockout mice might be helpful to elucidate the mechanisms of carcinogenicity. The other issues concern the development of screening or alternative methods. In the future, *in silico* and *in vitro* approaches will be powerful tools for screening genotoxic and carcinogenic potentials of a number of chemicals/agents.

Key words: food, carcinogenicity, assessment, risk factor

Introduction

Since carcinogenicity is recognized as one of the most serious toxicities, its refined assessment is necessary to prevent human health from cancer development. It has been reported that a number of chemicals and mixtures are known to be carcinogenic to humans and/or rodents¹. Carcinogenic potentials are assessed by I

Received: 15 June 2013; Accepted: 26 June 2013

* Corresponding author: E-Mail: nishikaw@nihs.go.jp

The contents of this article reflect solely the view of the author(s).

Abbreviations: ADI, acceptable daily intake; ALARA, as low as reasonably achievable; BMDL, benchmark dose limit; CAR, constitutive androstane receptor; IARC, International Agency for Research on Cancer; ICH, International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use; IPCS, International Programme on Chemical Safety; ILSI/HESI, International Life Sciences Institute/Health and Environmental Sciences Institute; MOA, mechanism of action; MOE, margin of exposure; NOAEL, no-observed-adverse-effect-level; NOGEL, no-observed-genotoxic-effect level; OECD, Organisation for Economic Co-operation and Development; PPAR, peroxisome proliferator-activated receptor; SAR, structure-activity relationship; TTC, threshold of toxicological concern; WOE, weight of evidence

2

Food Safety also publishes risk assessments conducted by FSCJ in 3 article types (full report, executive summary and summary).

Shown on right is an excerpt from an executive summary on fluorine (Food Safety. 2013; 1(1): 70-72).

Food Safety publishes original articles, short communications, and reviews covering broad areas of food safety related to the risk assessment of foods.

Shown on left is an excerpt from a review article by A. Nishikawa. (Food Safety. 2013; 1(1): 2-11).

Fluorine

Executive Summary

Food Safety Commission of Japan
December 2012 – FS/1052/2012

The Food Safety Commission of Japan (FSCJ) was asked by the Ministry of Health, Labour and Welfare to assess the risks of chemical substances related to the revision of the standards and criteria for 'beverages.' Since fluorine is one of the substances, the risk assessment on fluorine and fluoride was conducted. The data used in the assessment include those from: acute toxicity tests in mice and rats, subacute toxicity tests in mice, rats, rabbits, dogs and pigs, chronic toxicity and carcinogenicity tests in mice, rats and rabbits, neurotoxicity tests in mice and rats, immunotoxicity tests in mice, rats and rabbits, reproductive and developmental toxicity tests in mice and rats, genotoxicity tests, and epidemiological studies and others. Although fluorine has been considered to be an essential element, clear evidence has not been presented. Moreover, its daily minimum requirement has not been established. Epidemiological studies to examine the carcinogenicity of fluoride in drinking water have been conducted, but failed to provide clear evidence of carcinogenicity in humans. Carcinogenicity has not been clearly shown in laboratory animals, either. Fluoride has been reported to be weakly genotoxic *in vitro* studies using cultured mammalian cells. It is, however, reported that *in vivo* DNA damage tests have not indicated genotoxicity. Taken together, it was considered that fluorine has no genotoxicity relevant to human health. Hence, it was concluded that it is appropriate to specify a tolerable daily intake (TDI) of fluorine in terms of non-carcinogenic toxicity. Based on an epidemiological study of 5,800 children from 12 to 14 years old in the United States, a concentration of 1.0 ppm at which effect was not observed, was taken as a base. Given that the body weight of a child is 20 kg and the amount of water that a child drinks per day is 1 L, no-observed-adverse-effect-level (NOAEL) was calculated to be 0.05 mg/kg body weight per day. Since this value was that obtained from the study of susceptible population, it was considered that this value could be taken as TDI without applying uncertainty factors. As a conclusion, FSCJ specified the TDI of fluorine to be 0.05 mg/kg body weight per day.

Biological Effects of Fluorine and Fluoride

Fluorine has been considered to be an essential element though clear evidence has not been presented. Moreover, its daily minimum requirement has not been established. Fluoride that dissolves in drinking water at low concentrations is known to have an anticaries effect, while it may cause adverse effects on tooth enamel such as dental fluorosis. In addition, other effects such as skeletal fluorosis and an effect on bone fracture in humans have been reported. In laboratory animals, reproductive and developmental toxicities and effects on the nervous system have been reported. Thus, epidemiological studies on these health effects have been conducted.

This is an English translation of excerpts from the original full report.

The original full report is available in Japanese at <http://www.fsc.go.jp/fscis/evaluationDocument/show/kya20030703211>.

Since fluorine usually exists as fluorides, the health effects of the compounds were assessed.

Acknowledgement: The FSCJ wishes to thank the members of the Working Group on Beverages for the preparation of this report. The FSCJ also acknowledges the members of Expert Committee on Chemicals and Contaminants for their effort to provide this scientific output.

Food Safety - The Official Journal of Food Safety Commission of Japan is a peer-reviewed open-access electronic online journal of English published quarterly by the FSCJ. The journal will feature four types of articles: Original Articles, short communications, reviews, and risk assessments conducted by FSCJ.

Scope of the journal

The aim of the publication of Food Safety is to gather and disseminate scientific and technological information in the field of food safety on human health, and thereby facilitate the development of science and technology for risk assessments of foods. The journal publishes original articles, short communications, and reviews covering broad areas of food safety related to the risk assessment of foods as well as risk assessments conducted by FSCJ. Papers dealing with the following areas are particularly welcome: (1) pathogenicity or toxicity of biological, physical, or chemical agents concerning food safety; (2) occurrence of biological, physical, or chemical agents in the food chain with emphasis on food safety; (3) epidemiology or control of food-borne illnesses; and (4) safety evaluation of novel foods including nanomaterials, genetically modified organisms, etc. In addition to these areas, papers on the methodology of risk assessments concerning food safety are encouraged.

Disclaimer

The publication of original articles, short communications and reviews in Food Safety does not mean that the FSCJ condones, endorses, approves, or recommends the use of any products, services, materials, methodology, or policies stated therein. Conclusions and opinions in these articles are those of the individual authors only and do not reflect the policies or view of the FSCJ.

Editor in Chief Susumu Kumagai (FSCJ)

Associate Editors Katsue Ishii (FSCJ), Kiyoko Kamiyasuhira (FSCJ), Kunitoshi Mitsumori (FSCJ), Masatsune Murata (FSCJ), Hiroshi Satoh (FSCJ), Yasushi Yamazoe (FSCJ)

Editorial Board G. Endo (Osaka City University Medical School, Japan), R. Hasegawa (Pharmaceuticals and Medical Devices Agency, Japan), T. Hayakawa (Kinki University, Japan), A. Hirose (National Institute of Health Sciences, Japan), K. Imaida (Kagawa University, Japan), H. Karaki (Kurashiki University of Science and the Arts, Japan), A.-K. Lundebye (National Institute of Nutrition and Seafood Research, Norway), A. Martin (European Food Safety Authority, Italy), S. Miyazaki (National Institute of Animal Health, Japan), H. Mizusawa (Tokyo Medical and Dental University, Japan), M. Naya (BioSafety Research Center, Japan), A. Nishikawa (National Institute of Health Sciences, Japan), T. Nohmi (National Institute of Biomedical Innovation, Japan), K. Ogawa (National Institute of Health Sciences, Japan), H. Ozaki (University of Tokyo, Japan), T. Sakai (Azabu University, Japan), J. Sawada (Pharmaceuticals and Medical Devices Agency, Japan), T. Sekizaki (University of Tokyo, Japan), M. Shimizu (University of Tokyo, Japan), K. Shinagawa (Iwate University, Japan), V. Silano (Medical School, II University of Rome, Italy), Y. Sugita-Konishi (Azabu University, Japan), H. Tsubone (University of Tokyo, Japan), S. Tsuda (Iwate Institute of Environmental Health Sciences, Japan), T. Umemura (National Institute of Health Sciences, Japan), H. Verhagen (National Institute for Public Health and the Environment, The Netherlands), J. Yamate (Osaka Prefecture University, Japan), T. Yoshizawa (Ehime University, Japan).

Editorial Office

Chief Staff Isao Tojo (FSCJ)

Staff Ryusuke Matsuoka (FSCJ), Emi Takagi (FSCJ), Megumi Kozai (FSCJ), Masahiko Matsumoto (FSCJ)

Address The Food Safety Commission, Cabinet Office, Akasaka Park Bld. 22F, 5-2-20 Akasaka, Minato-ku, Tokyo 107-6122, Japan.

For further information Editorial office of the Food Safety journal, E-mail: fs-journal@cao.go.jp
Please go to the following URL to see Food Safety journal on J-STAGE:

<https://www.jstage.jst.go.jp/browse/foodsafetyfscj>

Call for Papers

We welcome to accept your manuscript for submission to *Food Safety*, a peer-reviewed open-access online journal in English. Please send your article through an e-mail attachment to the editorial office (fs-journal@cao.go.jp).

Submission of manuscripts

All manuscripts must be submitted to the publication office of FSCJ by e-mail (fs-journal@cao.go.jp) in attached files. When submitted, the text of manuscripts should be saved in both MS-Word and PDF files, and each figure and each table of manuscripts should be saved in a PDF file. In an accompanying letter, authors should state that the manuscript, or parts of it, have not been and will not be submitted elsewhere for publication.

Copyright

The copyright for any article appearing in this journal will be held by FSCJ. No part of the publication may be reproduced or transmitted in any form, or by any means, electronic or mechanical, including photocopy, recording, or any information storage and retrieval system, except in limited quantities for the non-commercial purposes of scientific or educational advancement, without permission in writing from the Journal Editorial office of FSCJ.

Editorial review

Manuscripts are peer-reviewed by two reviewers. If there is an inconsistent evaluation between two reviewers, a third reviewer is selected. Decisions of the Editors are final. Authors will receive page proofs of their article before publication, and should answer all queries and carefully check all editorial changes at this point.

See more details at:

Food Safety website:

<https://www.jstage.jst.go.jp/browse/foodsafetyfscj>

Instructions to authors:

<https://www.jstage.jst.go.jp/jstage/edit/foodsafetyfscj/pdf/rule.pdf>

For further information, please contact the editorial office:

Food Safety editorial office: fs-journal@cao.go.jp

Table of Contents

Volume 1, Number 1
December 2013

<i>From Editor-in-Chief</i> <i>Susumu Kumagai</i>	1
Reviews (Invited) Carcinogenicity Assessment for Risk Factors in Food: Current Issues and a Proposal <i>Akiyoshi Nishikawa</i>	2
Thirty-five Years of Research on Deoxynivalenol, a Trichothecene Mycotoxin: with Special Reference to Its Discovery and Co-occurrence with Nivalenol in Japan <i>Takumi Yoshizawa</i>	12
Identification and Evaluation of Potentially Genotoxic Agricultural and Food-related Chemicals <i>Makoto Hayashi, Masamitsu Honma, Motoko Takahashi, Atsuko Horibe, Jin Tanaka, Mai Tsuchiya, Takeshi Morita</i>	32
Intestinal Transmission of Prions and Role of Exosomes in Enterocytes <i>Yasuhisa Ano, Akikazu Sakudo, Ryuta Uraki, Juri Kono, Masayoshi Yukawa, Takashi Onodera</i>	43
Fumonisin Toxicity and Mechanism of Action: Overview and Current Perspectives <i>Kenneth A. Voss, Ronald T. Riley</i>	49
Risk Assessment Report: Beverages Executive Summary Fluorine <i>Food Safety Commission of Japan</i>	70

Volume 2, Number 1
March 2014

Risk Assessment Report: Apparatuses, Containers and Packages Executive Summary Bis(2-ethylhexyl)phthalate (DEHP) <i>Food Safety Commission of Japan</i>	1
Erratum: Bis(2-ethylhexyl)phthalate (DEHP)	e1
Risk Assessment Report: Microorganism and Viruses Executive Summary <i>Listeria monocytogenes</i> in foods <i>Food Safety Commission of Japan</i>	5
Risk Assessment Report: Veterinary Medicinal Products Summary Moxidectin <i>Food Safety Commission of Japan</i>	9
Risk Assessment Report: Food Additives Summary Advantame <i>Food Safety Commission of Japan</i>	11
Summary Polyvinylpyrrolidone <i>Food Safety Commission of Japan</i>	12
Risk Assessment Report: Feed Additives and Pesticides Summary Ethoxyquin <i>Food Safety Commission of Japan</i>	14
Risk Assessment Report: Pesticides Summary Fenoxasulfone <i>Food Safety Commission of Japan</i>	16

Review (Invited) Possible Carcinogenic Mechanisms Underlying Renal Carcinogens in Food <i>Takashi Umemura</i>	17
Risk Assessment Report: Veterinary Medicinal Products Summary Methyl Pyruvate and Marinedip <i>Food Safety Commission of Japan</i>	31
Risk Assessment Report: Pesticides Summary Quinoclamine <i>Food Safety Commission of Japan</i>	33
Risk Assessment Report: Veterinary Medicinal Products Summary Orbifloxacin <i>Food Safety Commission of Japan</i>	34
Risk Assessment Report: Pesticides Summary Ethoxysulfuron <i>Food Safety Commission of Japan</i>	36

Review (Invited) Norovirus and Foodborne Disease: A Review <i>Hiroshi Ushijima, Tsuguto Fujimoto, Werner EG Müller, Satoshi Hayakawa</i>	37
Risk Assessment Report: Prions Full Report Consideration of Risk Variations in Japan Derived from the Proposed Revisions of the Current Countermeasures against BSE <i>Food Safety Commission of Japan</i>	55
Risk Assessment Report: Pesticides Executive Summary Malathion <i>Food Safety Commission of Japan</i>	129
Summary Propiconazole <i>Food Safety Commission of Japan</i>	132
Risk Assessment Report: Veterinary Medicinal Products Summary Metronidazole <i>Food Safety Commission of Japan</i>	134
Risk Assessment Report: Pesticides Summary Flumioxazin <i>Food Safety Commission of Japan</i>	136
Risk Assessment Report: Apparatuses, Containers and Packages Summary Dibutyl Phthalate (DBP) <i>Food Safety Commission of Japan</i>	138
Risk Assessment Report: Genetically Modified Foods and Feeds Summary Stearidonic Acid Producing Soybean MON87769 Line <i>Food Safety Commission of Japan</i>	140



Food Safety website

<https://www.jstage.jst.go.jp/browse/foodsafetyfscj>

About Food Safety Commission

Food Safety Commission of Japan (FSCJ) was established on July 1st, 2003, as a part of Japanese Cabinet Office, based on its founding regulation of Food Safety Basic Act. Its mission was set as ‘implementing science-based risk assessments in an objective, neutral and impartial manner’. As an independent risk assessor, FSCJ’s role is different by nature from that of risk managers, such as the Ministry of Health, Labour and Welfare (MHLW), the Ministry of Agriculture, Forestry and Fisheries (MAFF), and the Consumer Affairs Agency (CAA), in that the responsibility of those risk managers are to develop administrative measures and regulations of food safety. To visit our home page, please follow this link: <http://www.fsc.go.jp/english/index.html>



Food Safety Commission of Japan

<http://www.fsc.go.jp/english/index.html>

**Address: The Food Safety Commission, Cabinet Office,
Akasaka Park Bld. 22F, 5-2-20 Akasaka,
Minato-ku, Tokyo 107-6122, Japan**

Fax: +81-3-3584-7390