

(別紙) 研究成果の概要 (英文)

Title of research project	Study on application of in silico evaluation method to risk assessment of trace level chemicals unintentionally contained in food.
Research project number	1803
Research period	FY 2018 – 2019
Name of principal research investigator (PI)	Atsushi Ono

Abstract/Summary

Various chemicals, such as leachable from food containers, can be unintentionally included in food though usually trace amounts. For the risk assessment of such chemicals, sufficient toxicity test information has not been obtained and sometime toxicity test is difficult to conduct. Recently, in silico methods based on toxicological database of “similar” chemicals with structures, physicochemical property etc. are being accepted on the risk assessment in Europe and the United States. Such in silico methods are considered to be useful in the risk assessment by the Food Safety Commission.

In this project, to test reliability and applicability of in silico methods expected to be useful and develop guidance for in silico evaluation, for chemicals which related food packaging as target of risk assessment, in silico evaluation for Ames mutagenicity and NO(A)ELs of repeated dose was conducted and compared the available toxicological information which was collected in this project. For Ames mutagenicity, result of in silico prediction integrating two different (Q)SAR method, rule base and statistical base, shown high specificity indicated sufficient conservativity and reliability of in silico method in application on regulatory risk assessment. For prediction of the NO(A)ELs of repeated dose, read-across from similar chemicals, i.e. category approach, is seems useful if information for similar chemicals is available. To search similar chemicals, the combination of whole structural similarity with physicochemical properties, Cramer class and also substituents that contribute to toxicity was useful. The reliability of read-across may be affected by MoA/AOP, metabolism, etc., thus, availability of detailed information for toxicity and also assessment of uncertainty is an issue. For risk assessment of repeated dose toxicity, TTC (Threshold of Toxicological Concern) approach is also useful. NO(A)ELs of all chemicals evaluated in this project were higher than TTC of each of Cramer class. Availability of reliable information for

exposure is issue for conduct risk assessment using TTC approach. Finally, based on the findings obtained from evaluation in this project, we developed “General consideration for applying the in silico methods in the safety evaluation of food-related chemical substances.” and proposed as a reference for developing guidance in future.

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1. List of papers published on the basis of this research

None

2. List of presentations based on this research

A. Ono, M. Nakamoto, N. Iizuka and M. Isozaki: Development of new risk assessment guideline of Food Contact Materials based on the TTC concept in Food Safety Commission of Japan. *IUTOX 15th International Congress of Toxicology (ICTXV) Meeting* (2019. July, Hawaii)

K. Chikazawa, A. Ono: A study on the prediction of a 28-day repeated-dose toxicity from a 14-day study based on the structural classification of chemical substances. The 46th Japan Society of Toxicology (2019. June, Tokushima)

3. The number and summary of patents and patent applications

None

4. Others (awards, press releases, software and database construction)

None