

This is a provisional English translation of an excerpt from the original full report.

Risk Assessment Report

Arsenic in foods

(Chemicals and contaminants)

Food Safety Commission of Japan (FSCJ)

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ABSTRACT

FSCJ conducted risk assessment of arsenic in food, as a Self-Tasking assessment and as a risk assessment related to revision of the standards for beverages, based on data from various studies, epidemiological studies and others.

The data used in the assessment are on toxicokinetics, acute toxicity, chronic toxicity, carcinogenicity reproductive and developmental toxicity, genotoxicity and others of inorganic arsenic compounds, organic arsenic compounds and synthesized organic arsenic compounds.

According to the epidemiological studies in the area with a long term intake of drinking water contaminated with arsenic, noncarcinogenic effects of inorganic arsenic exposure, such as skin lesions, neurodevelopmental, reproductive and developmental effects, were observed depending on the inorganic arsenic concentration in drinking-water. Among these, skin lesions were the adverse effects observed at the lowest concentration. The lowest observed adverse effect level (LOAEL) was 7.6-125 µg/L and the 95% lower confidence limit of benchmark concentration at which the incident rate increases 5% (BMCL₀₅) was 19.5-54.1 µg/L.

Also, cancers such as lung tumors, urinary bladder tumors and others, and genotoxicity such as chromosomal aberration due to inorganic arsenic exposure were observed in humans. Although implication of genotoxicity in the carcinogenic effect of inorganic arsenic exposure is suggested, none of the currently available data is conclusive for the direct effect of arsenic on DNA. In addition, animal studies in rodents suggest that the carcinogenesis by arsenic exposure is attributable to DNA damage induced by indirect interaction of arsenic but not to the direct interaction of arsenic with DNA such as production of an adduct. Although a threshold mechanism may be assumed on the basis of these points, the data is insufficient at this particular stage.

Hence, FSCJ concludes that the threshold of carcinogenicity in arsenic exposure could not be determined.

In this assessment, the no observed adverse effect level (NOAEL) (or LOAEL) and the 95% lower confidence limit of benchmark dose (BMDL) of inorganic arsenic were calculated by adding arsenic intake via diet to the intake by drinking-water based on the above mentioned epidemiologic surveys of long-term intake of arsenic contaminated water as follows. LOAEL of 4.3-5.2 $\mu\text{g}/\text{kg}$ bw/day and BMDL_{05} of 4.0-4.2 $\mu\text{g}/\text{kg}$ bw/day for skin lesions; NOAEL of 3.0-4.1 $\mu\text{g}/\text{kg}$ bw/day for effect on the nervous system (decreased IQ); NOAEL of 8.8-11.1 $\mu\text{g}/\text{kg}$ bw/day for effect on reproduction and development; NOAEL of 4.1-4.9 $\mu\text{g}/\text{kg}$ bw/day for lung tumors; NOAEL of 5.0-12.1 $\mu\text{g}/\text{kg}$ bw/day and BMDL_{01} of 9.7-13.5 $\mu\text{g}/\text{kg}$ bw/day for urinary bladder tumors.

However, in calculation of the NOAEL or BMDL based on the epidemiological studies, daily intake of inorganic arsenic generally tends to be underestimated, because food items used to estimate arsenic intake were limited. Moreover, in some cases of high exposure through drinking water, the exposure through food is even higher. Thus FSCJ considered the estimated values to be possible with non-negligible variation.

Meanwhile, the estimated intake of inorganic arsenic in the cases of people with normal lifestyles and not being exposed excessively by accident or contamination was 0.130-0.674 $\mu\text{g}/\text{kg}$ bw/day as the average from several duplicated diet studies in Japan. The survey by FSCJ in 2013, which is one of these diet studies, showed a mean value of 0.315 $\mu\text{g}/\text{kg}$ bw/day and 95 percentile value of 0.754 $\mu\text{g}/\text{kg}$ bw/day.

Each value of NOAEL/BMDL and the estimated intake of inorganic arsenic probably contain uncertainties. However, both values are close. Thus, some of the Japanese population with high exposure may have an intake above the value of NOAEL or BMDL that are estimated in this assessment.

It is necessary to examine whether it is appropriate to estimate the total inorganic arsenic intake from the arsenic concentration in drinking-water of the arsenic contaminated area. It is also necessary to examine whether it is appropriate to apply the results of dose-response assessment based on surveys where exposure through drinking water is substantial in Japan where the people scarcely intake arsenic from drinking-water. Also, there are still many problems to be solved to conduct a detailed risk assessment in which tolerable daily intake (TDI) is evaluated by estimating NOAEL or BMDL and unit risk is calculated. For example, the effects from the several factors associated with the difference in dietary habits, environment, sanitation, medical care systems, and lifestyle, may be related to the difference in health effects of inorganic arsenic exposure. The effects of smoking or other chemical compounds on health effects which derived from inorganic arsenic exposure are mostly unknown.

If there is a lack of data on carcinogenic mechanisms which is required for hazard assessment, and if the uncertainty in exposure assessment is high, unknown factors have been involved in the risk assessment even when the latest scientific evidences are used. These situations are considered to be the cause of the gap between the estimation and reality. If there is a discrepancy between the result of the assessment on a hazardous substance and the current situation in Japan, the real situation should be taken as a basis for the consideration.

Therefore, epidemiological studies on the population with arsenic exposure in everyday life and studies on mechanisms for the toxicity will be required to support the exposure assessment or the dose-response data, with evidence such as the actual exposure situation in Japan and the arsenic exposure through food intake. Also, further information on the toxicities of organic arsenic compounds are required because the data on toxicological effects of organic arsenic compounds for assessment of food safety risk are insufficient.