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

Risk Assessment Report

Ochratoxin A

(Natural toxins and mycotoxins)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted a risk assessment of ochratoxin A (hereinafter referred to as OTA) as a Self-Tasking Risk assessment.

The data used in the assessment are on: toxicokinetics, acute toxicity, subacute toxicity, chronic toxicity, carcinogenitiсy, reproductive and developmental toxicity, genotoxicity, neurotoxicity and immunotoxicity.

OTA is a mycotoxin produced by several fungal species such as *A. ochraceus* and *P. verrucosum*, which occur mainly in stored foods. OTA contamination has been found in various food commodities including cereal, coffee, cocoa, beer and wine.

Nephrotoxicity was observed in all of the animal species tested in the subacute toxicity study. Marked developments of karyomegaly and cytomegaly as well as tubular atrophy and degeneration were observed in proximal tubules in the outer stripe of the outer medulla. In rats and pigs the dose-dependent effects of OTA on kidneys and also the relationship with the duration of exposure were shown.

In chronic toxicity/carcinogenicity study of OTA, development of tumors were observed mainly at the outer stripe of the outer medulla in male rats after oral administration in rodent.

In genotoxicity studies of OTA, chromosome aberration was observed both *in vitro* and *in vivo*; however, gene point mutations were not detected. After reviewing the results of various toxicological studies, FSCJ concluded that OTA is a non-genotoxic carcinogen, acting indirectly on DNA, thus its tolerable daily intake (TDI) is reasonably specified.

Regarding non-carcinogenic toxicity of OTA, the effect observed at the lowest dose in various toxicological studies was the reduced capacity to concentrate urine and the degenerative changes in the tubular epithelial cells observed in a 120-day subacute toxicity study in pigs. The lowest observed adverse effect level (LOAEL) in these studies was 8 µg/kg bw/day. FSCJ specified a TDI of 16 ng/kg bw/day, applying an uncertainty factor of 500 (10 for species difference, 10 for individual difference and 5 for the use of LOAEL based on irreversible renal failure indices) to the LOAEL.

Regarding carcinogenicity of OTA, FSCJ considered a TDI based on the no observed adverse effect level (NOAEL). FSCJ adopted the NOAEL of 21 µg/kg bw (administered 5 times a week, equivalent to 15 µg/kg bw/day) derived froma 2 year carcinogenicity study in rats performed by The National Toxicology Program (NTP). FSCJ specified TDI of 15 ng/kg bw/day, applying a safety factor of 1000 (10 for species difference, 10 for individual difference and 10 for carcinogenicity) to the NOAEL. The estimated exposure levels of OTA in Japan for average (50 percentile) and high risk consumers (95 percentile) are 0.14 ng /kg bw/day and 2.21 ng/kg bw/day, respectively. These estimates indicate that the OTA exposure level for high risk consumers are still below the TDI specified above. Therefore, FSCJ considers that risk to human health from the intake of OTA through food is insignificant in Japan.

The major OTA producers in agricultural and food products grow under different environmental conditions, and the level of contamination with OTA is influenced by climatic and other conditions. Therefore, risk management institutions should monitor the situation of OTA contamination in foods and review the standards and criteria as necessary.