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

Risk Assessment Report

2,3-Diethylpyrazine
(Food Additives)

Food Safety Commission of Japan (FSCJ)
August 2014

ABSTRACT

FSCJ conducted a risk assessment of 2,3-diethylpyrazine (CAS No.15707-24-1), as an additive, based on results from various studies bearing in mind the usage for a flavor.

Data used in the assessment includes genotoxicity and repeated dose toxicity.

This additive, 2,3-diethylpyrazine, has no apparent toxicity relevant to human health based on the results of studies including the genotoxicity and repeated dose toxicity. In addition, FSCJ confirmed that the additive (flavouring) was categorized into Structural class II, based on Method of safety assessment on internationally commonly used flavorings[1]. The safety margin (11,000～22,000) exceeds 1,000 which is regarded as the appropriate safety margin for a 90-day repetitive dose toxicity study. The predicted amount of intake (1~2 μg/person/day) is also lower than the acceptable daily intake of Structural class II (540 μg/person/day).

Hence, FSCJ concluded that 2,3-diethylpyrazine, an additive (flavoring), has no concern relevant to human health when it is used for the purpose of flavoring food.

Supplementary note on genotoxicity

In the micronucleus test using the medium dose of 2,3-diethylpyrazine (125 mg/kg body weight/day) and the high dose (250 mg/kg body weight/day), MNPCE (Micronucleated polychromatic erythrocytes) has been observed. The applicant considered the appearance of MNPCE as the secondary effect attributable to the chemical-induced hypothermia. Although body temperature of the test animals was not measured in the relevant micronucleus test, FSCJ granted the interpretation in consideration with hypothermia data reported by Boulet (2012).
Regarding the occurrence of MNPCE with the low dose of 2,3-diethylpyrazine (62.5 mg/kg body weight/day) in the micronucleus test, FSCJ could not verify it to be the hypothermic effect due to the lack of body temperature data of the test animals. Nevertheless FSCJ considered the trivial biological

[1] Report of Working group on safety assessment method of flavorings, November 4, 2003

significance of the occurrence of MNPCE in this low dose. The 0.24% frequency of MNPCE occurrence in the low dose was much lower than that in the medium dose (0.70%) or that in the high dose (0.62%), and also within levels of the frequencies (0.05~0.24%) obtained for the negative control group of micronucleus tests at the test facility.

Positive results suggesting the chromosomal structural changes were obtained from chromosomal aberration tests in cultured mammalian cells. The direct DNA damage is unlikely to occur *in vivo* because of the abovementioned reasons. FSCJ concluded that the threshold could be specified for a slight increase in polyploid cells without showing the dose-dependency. Human exposure to 2,3-diethylpyrazine as an additive for flavoring (estimated amount of intake) is so low and will never reach to the exposure to induce numerical chromosome aberration or decrease in body temperature. Thus, 2,3-diethylpyrazine has no concern relevant to human health as used for the purpose of flavoring food.

Therefore, FSCJ concluded that 2,3-diethylpyrazine has no genotoxicity relevant to human health as long as it is used for the purpose of flavoring food.