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

Risk Assessment Report

Polyvinylimidazole - polyvinylpyrrolidone copolymers (PVI/PVP copolymer)

(Food Additives)

Food Safety Commission of Japan (FSCJ)
December 2020

ABSTRACT

The FSCJ conducted a risk assessment of polyvinylimidazole - polyvinylpyrrolidone copolymers (PVI/PVP copolymer) (CAS No. 87865-40-5), an additive used as a filter aid for wine, based on results from submitted documents.

The additive "PVI/PVP copolymer" contains impurities such as 1-vinyl-2-pyrrolidone (NVP), 1-vinylimidazole (NVI), 1,3-divinylimidazolidine-2-one (DVI), 2-pyrrolidone and imidazole. Among them, DVI further decomposes to acetaldehyde, urea and ethylene glycol in wine. However, from the fact that the residual amounts of these decomposition compounds are low enough, the FSCJ judged that acetaldehyde, urea and ethylene glycol from DVI pose no concern about their safety as long as "PVI/PVP copolymer" is appropriately used according to the proposed "Standards for Use" by the Ministry of Health, Labour and Welfare (MHLW).

Consequently, the FSCJ selected the study results of PVI/PVP copolymer and its impurities, NPV, NVI, 2-pyrrolidone and imidazole to assess the safety of the additive "PVI/PVP copolymer" in the assessment.
The study results used in the evaluation cover the toxicokinetics, genotoxicity, acute toxicity, repeated dose toxicity, carcinogenicity, and reproductive and developmental toxicity of "PVI/PVP copolymer," NVP, NVI, 2-pyrrolidone, and imidazole.
The FSCJ carried out an evaluation based on the Margin of Exposure (MOE) for the following reasons: (1) "PVI/PVP copolymer" is removed before the final food products are completed; and (2) the intake of its impurities would be small since the upper limits are set ranging from 2 μg to 50 μg/g of "PVI/PVP copolymer" in the proposed "Specifications of the additive." Moreover, the FSCJ considered that the estimated intake would be overestimated in this assessment.

1. Polyvinylimidazole - polyvinylpyrrolidone copolymers ("PVI/PVP copolymer")

Absorption from gastrointestinal tract would be negligible due to its insolubility, though sufficient findings could not be obtained from the study of toxicokinetics of "PVI/PVP copolymer."

"PVI/PVP copolymer" had no particular genotoxicity relevant to human health.

It was considered that the identified NOAEL of "PVI/PVP copolymer" was 1,000 mg/kg bw per day, the highest dose in the data of 28-day repeated dose oral study in rats.

The estimated daily intake ('EDI') of "PVI/PVP copolymer" was estimated to be 0.437 mg/kg bw per day under overestimated assumption.

The FSCJ judged that the additive "PVI/PVP copolymer" has no safety concern as long as used appropriately because there is a sufficient margin between the NOAEL (1,000 mg/kg bw per day) and the EDI.

2. 1-Vinyl-2-pyrrolidone (NVP)

NVP plasma concentration reached the Cmax at 0.25 ~ 3 hours and more than 90 % of NVP was excreted within 48-hours after single oral administration in rats and dogs. In addition, NVP was assumed to be hydrolyzed mainly into 2-pyrolidone and acetaldehyde, and the hydrolysis rate was faster under acidic conditions. The FSCJ considered that NVP would be rapidly absorbed and excreted after oral administration, and its bioaccumulation would be low.

NVP had no particular genotoxicity relevant to human health.

It was considered that the identified NOAEL of NVP was 7.5 mg/kg bw per day, the highest dose in the data of the 3-month exposure of rats through drinking water.

The EDI of NVP derived from "PVI/PVP copolymer" was estimated to be 2.19×10^{-6} mg/kg bw per day, which value was calculated from the limit specified in the proposed "Specifications of the additive" by the MHLW.

The FSCJ judged that the impurity NVP has no safety concern as long as "PVI/PVP copolymer" is used appropriately as an additive, because there is a sufficient margin between the NOAEL (7.5 mg/kg bw per day) and the EDI.

3. 1-Vinylimidazole (NVI)

No test results of the toxicokinetics of NVI were submitted.

NVI had no particular genotoxicity relevant to human health.

It was considered that the identified NOAEL of NVI was 5 mg/kg bw per day from the test results of repeated dose toxicity and reproductive/developmental toxicity in rats.

The EDI of NVI derived from "PVI/PVP copolymer" was estimated to be 4.37×10^{-6} mg/kg bw per day, which value was calculated from the limit specified in the proposed "Specifications of the additive" by the MHLW.

The FSCJ judged that the impurity NVI has no safety concern as long as the additive "PVI/PVP copolymer" is used appropriately as an additive, because there is a sufficient margin between the NOAEL (5mg/kg bw per day) and the EDI.

4. 2-Pyrrolidone

No test results of the toxicokinetics of 2-pyrrolidone were submitted.

2-Pyrroridone had no particular genotoxicity relevant to human health.

It was considered that the identified NOAEL of 2-pyrrolidone was 190 mg/kg bw per day from the test results of repeated dose toxicity and reproductive/developmental toxicity in rats.

The EDI of 2-pyrrolidone derived from "PVI/PVP copolymer" was estimated to be 2.19×10^{-5} mg/kg bw per day, which value calculated from the limit specified in the proposed "Specifications of the additive." of the MHLW.

The FSCJ judged that the impurity 2-pyrrolidone has no safety concern as long as the additive "PVI/PVP copolymer" is used appropriately as an additive, because there is a sufficient margin between the NOAEL (190mg/kg bw per day) and the EDI.

5. Imidazole

After oral administration, the plasma concentration of imidazole reached the maximum within 15 ~ 30 min and 2 hours in rats and humans, respectively, and the half-life was about 2 ~ 3 hours in humans. The FSCJ considered that imidazole is rapidly absorbed and excreted after oral administration, and has low accumulation.

Imidazole had no particular genotoxicity relevant to human health.

It was considered that the identified NOAEL of imidazole was 60 mg/kg bw per day from the test results of repeated dose toxicity and reproductive/developmental toxicity in rats.

The EDI of imidazole derived from "PVI/PVP copolymer" was estimated to be 2.19×10^{-5} mg/kg bw per day, which value was calculated from the limit specified in the proposed "Specifications of the additive" by the MHLW.

The FSCJ judged that the impurity imidazole has no safety concern as long as the additive "PVI/PVP copolymer" is used appropriately as an additive, because there is a sufficient margin between NOAEL (60 mg/kg bw per day) and the EDI.

Given all of the above assessment results of PVI/PVP and its impurities, the FSCJ concluded that this additive "PVI/PVP copolymer" has no safety concern as long as used appropriately.