

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

Risk Assessment Report

Ammonium Hydrogen Sulfite Water

(Food Additives)

Food Safety Commission of Japan (FSCJ) December 2020

ABSTRACT

The FSCJ conducted a risk assessment of ammonium hydrogen sulfite water (CAS No. 10192-30-0, a solution consisting mainly of ammonium hydrogen sulfite as an active substance), based on submitted documents. This is an additive used as a fermentation aid, a preservative and an antioxidant. The FSCJ decided to totally assess the risk of the additive "ammonium hydrogen sulfite water" based on the risk assessment of ammonium ion, sulfur dioxide (SO₂) and sulfites that are expected to be produced in our body after ingestion. The data used for the assessment were followings: toxicokinetics, genotoxicity, acute toxicity, repeated dose toxicity, reproductive-developmental toxicity, and carcinogenicity tests in animals, and scientific findings in human of SO₂ and sulfites.

Ammonium ion

The FSCJ did not evaluate toxicokinetics and toxicity of ammonium ions in this assessment, because safety of ammonium ions had been already assessed in the past, and thereafter new findings which should be considered were not found. Meanwhile, the FSCJ considered that the human intake of ammonium ions derived from the additive was negligible compared to the ammonium ions originated from meals. The FSCJ judged that ammonium ions derived from the additive "ammonium hydrogen sulfite water" are of no concern for food safety as long as it is used appropriately.

SO2 and sulfites

SO₂, and sulfites from the additive "ammonium hydrogen sulfite water" are absorbed as SO₂, sulfite ion or hydrogen sulfite ion from digestive tracts. The absorbed sulfite is oxidized by sulfite oxidase in liver, or metabolized during the formation process from sulfuric acid to sulfur trioxide radical. Sulfite oxidase activity in rats is higher than that in rabbits or monkeys, and the oxidation in rat liver is about 10 to 20 folds higher than that in human liver. It was also considered that the half-life of S-sulfonic acid detected after intake of sulfites was short and its accumulation was low. Further, most of ingested sulfites was considered to be excreted promptly into urine or feces as sulfuric acid.

SO₂, and sulfites had no genotoxicity relevant to human health.

Slight abnormality in the stomach and esophagus was observed in the groups orally administered more than 1% sodium pyrosulfite in pig 48-week toxicity study (Til et al., 1972). On the basis of this finding, the FSCJ identified the NOAEL of 71 mg/kg bw per day (SO₂) calculating from 0.5 % administered group in the study.

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The FSCJ judged that sodium pyrosulfite does not have carcinogenicity from the results of a two-year carcinogenicity study in mice (Tanaka et al., 1979) and of combined two-year repeated dose toxicity/reproductive toxicity/carcinogenicity study in rats (Til et al., 1972).

Scientific findings in human

Although scientific findings obtained do not specifically report the allergenicity of ammonium hydrogen sulfite in humans, the FSCJ considered that the allergenicity of SO₂ and sulfites, both derived from the additive "ammonium hydrogen sulfite water," cannot be ruled out. "Standards for Use of Food Additives "issued by MHLW stipulates that "ammonium hydrogen sulfate water" should not be used except in fruit juice and wine (excluding wine that has already finished fermentation) for winemaking. Accordingly, the FSCJ considered that this additive should be used exclusively for winemaking.

Taking the above into consideration, the FSCJ judged that the NOAEL of SO₂ and sulfites derived from "ammonium hydrogen sulfite water" was 71 mg/kg bw per day (SO₂).

The FSCJ estimated that the daily intake of SO₂ from wine would be 0.113mg/kg bw per day, based on the maximum amount (0.2g/L) of the additive "ammonium hydrogen sulfite water" stipulated in the proposed "Standards for Use of Food Additives" and the daily intake of wine (48.2 mL/person per day) in targeting people who have a drinking habit. Adding the current daily intake obtained according to the market basket survey to the above estimated intake 0.113 mg/kg from wine, the FSCJ calculated that the estimated daily intake (EDI) of SO₂ would be 0.116 mg/kg bw per day after "Standards for Use of Food Additives" is finalized. However, the FSCJ considered that actual intake of the additive "ammonium hydrogen sulfite water" would be less than the above EDI for the following reasons:

- "Ammonium hydrogen sulfite water" added to the juice or must¹ prior to or during fermentation generates SO₂, and then produces sulfurous acid by reacting with water. Sulfurous acid is effective to prevent the growth and oxidation of toxic microorganisms. It gradually disappears via vaporization and oxidation in the atmosphere.
- 2. It is known that sulfurous acid added before fermentation combines with solids such as fruit juice and that its contained amount decreases.
- 3. The amount of sulfurous acid has to be analyzed before and after the addition of sulfite, and confirmed whether the amount is appropriate, and the record of the use should be kept, when sulfite is used as additives. Therefore, the FSCJ considered that the use of additive "ammonium hydrogen sulfite water" is controlled appropriately in the production of wine.

Although the NOAEL was obtained from the toxicity studies, the FSCJ considered that the adverse effects were not serious because the findings in the studies were slight abnormalities in the stomach and esophagus. Accordingly,

¹ "Must" is defined as follows: Must ("young wine") is fresh crushed fruit juice (usually grape juice) that contains the skins, seeds, and stems of the fruit. It does not matter whether alcohol is contained.



this additive has no safety concern as long as used appropriately as an additive, judging from its nature, usage, actual intake, and the proposed "Standards for Use." The FSCJ concluded that it was unnecessary to specify an ADI for "ammonium hydrogen sulfite water."