FOOD SAFETY

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Mepanipyrim

Summary

Food Safety Commission of Japan

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of mepanipyrim (CAS No.110235-47-7), an anilinopyrimidine fungicide, based on results from various studies. Major adverse effects of mepanipyrim observed were hepatocellular hypertrophy, hepatocellular degeneration, and increased kidney weight in rats. Neither reproductive toxicity, teratogenicity nor genotoxicity was observed. Mepanipyrim (parent compound only) was identified as a chemical for the residue definition for dietary risk assessment in agricultural products. FSCJ adopted the no-observed-adverse-effect level (NOAEL) of 7.34 mg/kg bw/day, obtained in a two-year combined chronic/carcinogenicity study in rats, appropriate for specification of an acceptable daily intake (ADI). An ADI was thus specified as 0.073 mg/kg bw/day, applying a safety factor of 100 to the NOAEL. The lowest NOAEL for adverse effects that would be likely to be elicited by a single oral administration of mepanipyrim was 400 mg/kg bw obtained in an acute neurotoxicity study in rats. Consequently, FSCJ specified an acute reference dose (ARfD) of 4 mg/kg bw, applying a safety factor of 100 to the NOAEL.

Conclusion in Brief

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of mepanipyrim (CAS No.110235-47-7), an anilinopyrimidine fungicide, based on results from various studies.

The data used in the assessment include on the fate in animals (rats), fate in plants (tomatoes, apples, etc.), residues in crops, subacute toxicity (rats and dogs), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), and genotoxicity.

Major adverse effects of mepanipyrim observed were hepatocellular hypertrophy, hepatocellular degeneration, and increased kidney weight in rats. Neither reproductive toxicity, teratogenicity nor genotoxicity was observed.

Increased incidence of hepatocellular adenomas was observed in female rats in a two-year combined-chronic toxicity study. Increases in hepatocellular adenomas and carcinomas were also observed in a carcinogenicity study of both sexes of mice. A genotoxic mechanism was unlikely to be involved in the tumor induction from results of the genotoxicity and mechanistic studies. It was thus reasonably considered to set a threshold level in the assessment.

Mepanipyrim (parent compound only) was identified as a chemical for the residue definition for dietary risk assessment in agricultural products.

A no-observed-adverse-effect level (NOAEL) value of 7.34 mg/kg bw/day was obtained in a two-year combined chronic/carcinogenicity study in rats. In a two-generation reproductive toxicity study in rats, a NOAEL and a lowest-

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observed-adverse-effect level (LOAEL) were 3.62 mg/kg bw/day and 10.9 mg/kg bw/day, respectively. FSCJ adopted the value of 7.34 mg/kg bw/day as the NOAEL value of mepanipyrim appropriate for specification of an acceptable daily intake (ADI), considering the toxic profiles and duration of experiments of both studies. An ADI was thus specified as 0.073 mg/kg bw/day, applying a safety factor of 100 to the NOAEL.

The lowest NOAEL for adverse effects that would be likely to be elicited by a single oral administration of mepanipyrim was 400 mg/kg bw obtained in an acute neurotoxicity study in rats. Consequently, FSCJ specified an acute reference dose (ARfD) of 4 mg/kg bw, applying a safety factor of 100 to the NOAEL.