FOOD SAFETY

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Sedaxane

Summary

Food Safety Commission of Japan

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of sedaxane (CAS No.874967-67-6), a pyrazole carboxamide fungicide, based on results from various studies. Major adverse effects of sedaxane observed are decreased body weight gain, decrease in food intake, and centrilobular hepatocellular hypertrophy. Sedaxane did not show any neurotoxicity, teratogenicity, reproductive toxicity, genotoxicity and immunotoxicity. In a two-year combined chronic toxicity/carcinogenicity study in rats, increased incidence of uterine adenocarcinomas was observed. Increased incidence of hepatocellular tumors was also observed in an 80-week carcinogenicity test in mice. However, a genotoxic mechanism was unlikely to be involved in the tumor induction. It was thus considered possible to establish a threshold in the assessment. Based on the above results, only sedaxane (parent compound) was identified as the residue definition for dietary risk assessment in agricultural products. The lowest no-observed-adverse-effect level (NOAEL) in the toxicological studies was 11 mg/kg bw/day in a combined two-year chronic toxicity/carcinogenicity study in rats. Applying a safety factor of 100 to the NOAEL, FSCJ specified the acceptable daily intake (ADI) of 0.11 mg/kg bw/day. The lowest NOAEL for adverse effects resulted from a single oral administration of sedaxane was 30 mg/kg bw observed in an acute neurotoxicity study in rats. Applying a safety factor of 100 to the NOAEL, FSCJ specified 0.3 mg/kg bw as the acute reference dose (ARfD).

Conclusion in Brief

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of sedaxane (CAS No.874967-67-6), a pyrazole carboxamide fungicide, based on results from various studies.

The studies include the fate in animals (rats, goats and chickens), fate in plants (spring wheat and soybeans), residues in crops, subacute toxicity (rats, mice and dogs), subacute neurotoxicity (rats), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), and genotoxicity.

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In a two-year combined chronic toxicity/carcinogenicity study in rats, increased incidence of uterine adenocarcinomas was observed. Increased incidence of hepatocellular tumors was also observed in an 80-week carcinogenicity test in mice. However, a genotoxic mechanism was unlikely to be involved in the tumor induction. It was thus considered possible to establish a threshold in the assessment.

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