FOOD SAFETY

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Picoxystrobin

Summary

Food Safety Commission of Japan

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of picoxystrobin (CAS No. 117428-22-5), a strobilurin fungicide, based on results from various studies. Major adverse effects of picoxystrobin observed are decreased body weight gain, hepatocellular hypertrophy in mice, as well as mucosal hyperplasia and dilated mucosal gland of the duodenum in mice. No neurotoxicity, reproductive toxicity, teratogenicity, immunotoxicity or genotoxicity relevant to human health were observed. Although increased incidences of interstitial cell adenomas were observed in a two-year chronic toxicity/carcinogenicity study in rats, genotoxic mechanism was unlikely to be involved in the tumor induction, and therefore, FSCJ concluded that it is possible to establish a threshold dose in the assessment. Based on the above results, only picoxystrobin (parent compound) was identified as the residue definition for dietary risk assessment in agricultural products. The lowest no-observed-adverse-effect level (NOAEL) obtained was 4.6 mg/kg bw/day in a one-year chronic toxicity study in dogs. FSCJ specified the acceptable daily intake (ADI) of 0.046 mg/kg bw/day, applying a safety factor of 100 to the NOAEL. In an acute neurotoxicity study in rats, NOAEL was not obtained, but the lowest-observed-adverse-effect level (LOAEL) was 200 mg/kg bw. In developmental toxicity studies, NOAELs obtained for adverse effects possibly caused by a single oral administration of picoxystrobin were 25 mg/kg bw/day in rabbits and 30 mg/kg bw/day in rats. Considering those results comprehensively, FSCJ specified an acute reference dose (ARfD) of 0.2 mg/kg bw based on the LOAEL of 200 mg/kg bw obtained from an acute neurotoxicity study in rats, applying a safety factor of 1,000 (10 for species difference, 10 for individual difference, and 10 for the adopted LOAEL value).

Conclusion in Brief

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of picoxystrobin (CAS No. 117428-22-5), a strobilurin fungicide, based on results from various studies.

The studies include data on the fate in animals (rats), fate in plants (wheat and tomatoes), residues in crops, subacute toxicity (rats 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), immunotoxicity (rats and mice) and genotoxicity.

Major adverse effects of picoxystrobin observed are decreased body weight gain in rats, mice and dogs, and hepatocellular hypertrophy, mucosal hyperplasia and dilated mucosal gland of the duodenum in mice. Neither neurotoxicity, reproductive toxicity, teratogenicity, immunotoxicity nor genotoxicity relevant to human health were observed.

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Although incidence of Leydig cell tumor was increased in a two-year chronic toxicity/carcinogenicity study in rats, involvement of genotoxic mechanism was unlikely in the tumor induction. It is thus possible to establish a threshold dose in the assessment.

Only picoxystrobin (parent compound) was identified as the residue definition for dietary risk assessment in agricultural products from the data including residues in crops.

The lowest no-observed-adverse-effect level (NOAEL) obtained was 4.6 mg/kg bw/day in a one-year chronic toxicity study in dogs. FSCJ specified the acceptable daily intake (ADI) of 0.046 mg/kg bw/day, applying a safety factor of 100 to the NOAEL.

In an acute neurotoxicity study in rats, NOAEL was not obtained, but the lowest-observed-adverse-effect level (LOAEL) was 200 mg/kg bw. In developmental toxicity studies, NOAELs obtained for adverse effects possibly caused by a single oral administration of picoxystrobin were 25 mg/kg bw/day in rabbits and 30 mg/kg bw/day in rats. Considering those results comprehensively, FSCJ specified an acute reference dose (ARfD) of 0.2 mg/kg bw based on the LOAEL of 200 mg/kg bw obtained from an acute neurotoxicity study in rats, applying a safety factor of 1,000 (10 for species difference, 10 for individual difference, and 10 for the adopted LOAEL value).