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

Risk Assessment Report

Tepraloxydim

(Pesticides)

Food Safety Commission of Japan (FSCJ)

May 2015

ABSTRACT

FSCJ conducted a risk assessment of tepraloxydim (CAS No. 149979-41-9), an herbicide, based on summary reports submitted by the applicant and documents from governments of the US and Australia.

The data used in the assessment include fate in animals (rats, goats and chicken), fate in plants (soybeans, rapeseed oil and others), residues in crops, subacute toxicity (rats, mice and dogs), subacute neurotoxicity (rats), chronic toxicity (rats and dogs), carcinogenicity (rats and mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits) and genotoxicity.

Major adverse effects of tepraloxydim observed are decreased body weight gain, centrilobular hepatocellular hypertrophy in the liver, increased thyroid weights in dogs, atrophy of seminiferous tubules in dogs, epithelial hyperplasia in the urinary bladder in dogs and others. No neurotoxicity, developmental toxicity and genotoxicity relevant to human health were observed.

Total incidence of hepatocellular adenomas and carcinomas increased in male and female rats in a carcinogenicity study, but a genotoxic mechanism was unlikely to be involved in the tumor induction, and it was considered possible to establish a threshold dose in the assessment.

Tepraloxydim, at the dose with mataernal toxicity, caused fetal skeletal changes including filiformed tails in developmental toxicity tests in rats. No teratogenicity was observed in rabbits.

Based on the above results, tepraloxydim (parent compound only) and tepraloxydim and its metabolite[5] were identified as the residue definition for dietary risk assessment in agricultural and livestock products, respectively.

The lowest no-observed-adverse-effect level (NOAEL) obtained was 5 mg/kg bw/day in a two-year chronic toxicity study and a carcinogenicity study in rats. Applying a safety factor of 100 to the NOAEL, FSCJ specified an acceptable daily intake (ADI) of 0.05 mg/kg bw/day.

The lowest NOAEL for potential adverse effects of a single oral administration of tepraloxydim was 40 mg/kg bw/day in developmental toxicity tests in rats, which at the dose without mataernal toxicity caused fetal skeletal changes including delayed ossification of sternebrae and reduction in body weight gain. Consequently, for pregnant women or women who may be pregnant, FSCJ specified an aute reference dose (ARfD) of 0.4 mg/kg bw/day by applying a safety factor of 100 to the NOAEL. For a general population, ARfD of 1.6 mg/kg bw/day was derived based on lowest-observed-adverse-effect level (LOAEL) of 500 mg/kg bw/day in an acute neurotoxicity study in rats and applying a safety factor of 300 (10 for species difference, 10 for individual difference, and 3 for the adopted lowest-observed adverse effect level (LOAEL) value).