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

Risk Assessment Report

Tetraconazole

(Pesticides)

Food Safety Commission of Japan (FSCJ)
August 2015

ABSTRACT

FSCJ conducted a risk assessment of tetraconazole (CAS No. 112281-77-3), a triazole fungicide, based on results from various studies.

The data used in the assessment include the fate in animals (rats and goats), fate in plants (wheat and sugar beets), residues in crops, subacute toxicity (rats and mice), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), acute- and sub-acute neurotoxicity (rats), immunotoxicity (rats) and genotoxicity.

Major adverse effects of tetraconazole include centrilobular hypertrophy of hepatocytes in the liver, hypertrophy of tubular epithelial cells in renal cortex in dogs, and thickening of cranial bone. No immunotoxicity or genotoxicity were observed.

Locomoter activity was reduced in an acute neurotoxicity and subacute neurotoxicity study.

In a carcinogenicity study in mice, increased incidence of hepatocellular adenomas and hepatocellular carcinomas were observed, however a genotoxic mechanism was unlikely to be involved in tumor development. Therefore, FSCJ concluded that it is possible to establish a threshold dose for carcinogenicity.

Prolonged gestational period was observed in the reproductive toxicity study. Increased incidences of hydronephrosis and hydroureter were observed at maternal toxic dose in developmental toxicity study in rats. No teratogenicity was observed in rabbits.

Based on the data of the fate in animals and plants, tetraconazole (only parent compound) was identified as the residue definition for dietary risk assessment in agricultural products.

The lowest no-observed-adverse-effect level (NOAEL) obtained in all studies was 0.4 mg/kg bw/day in a combined chronic toxicity/carcinogenicity study in rats. FSCJ specified an acceptable daily intake (ADI) of 0.04 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.

The lowest NOAEL for potential adverse effects of a single oral administration of tetraconazole was 5 mg/kg bw/day in developmental toxicity studies of tetraconazole in rats. FSCJ specified an acute reference dose (ARfD) to be 0.05 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.