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

Risk Assessment Report

Metyltetraprole

(Pesticides)

Food Safety Commission of Japan (FSCJ)
July 2019

ABSTRACT

FSCJ conducted the risk assessment of methyltetraprole (CAS No.1472649-01-6), having a tetrazolinone skeleton, based on various documents.

The data used in the assessment include fate in animals (rats, goats and chicken), fate in plants (wheat and soybean), residues in crops, subacute toxicity (rats, mice and dogs), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproduction toxicity (rats), developmental toxicity (rats and rabbits), and genotoxicity. Kinetics was investigated in short- and long-term toxicity studies in rats and dogs. Short-term toxicity study of metabolite B and its toxicological information was provided in the documents.

Major adverse effect of methyltetraprole observed was only decreased feed intake in rabbits. Methyltetraprole showed none of neurotoxicity, carcinogenicity, adverse effects on reproductivity, teratogenicity and genotoxicity.

FSCJ attributed nonlinearity in area under the curve observed in the toxicity studies to saturated absorption and metabolic enzyme induction caused by increased administration dose.

From the above results, methyltetraprole (parent compound only) was identified as the relevant substance for the residue definition for dietary risk assessment in agricultural products, livestock products and fishery products.
The lowest value of the no-observed-adverse-effect level (NOAEL) in all tests was 250 mg/kg bw/day in a developmental toxicity study in rabbits. FSCJ specified an acceptable daily intake (ADI) of 2.5 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.
Since no potential adverse effects of a single oral administration of methyltetraprole was observed, FSCJ considered it unnecessary to specify an acute reference dose (ARfD).

Table 1. *Levels relevant to toxicological evaluation of methyltetraprole*

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
Rat	90-day subacute toxicity study	0, 2 000, 6 000, 20 000 ppm M: 0, 148, 438, 1 510 F: 0, 169, 509, 1 720	M: 1 510 F: 1 720	M: - F: -	M/F: No toxicity was observed.
	Two-year combined chronic toxicity/carcinogenicity study	0, 2 000, 6 000, 20 000 ppm M: 0, 83.9, 255, 852 F: 0, 112, 339, 1 190	M: 852 F: 1 190	M: - F: -	M/F: No toxicity was observed (No carcinogenicity)
	Two-generation reproductive activity study	0, 2 000, 6 000, 20 000 ppm PM: 0, 132, 409, 1 390 PF: 0, 154, 480, 1 540 F_1M: 0, 177, 524, 1 760 F_1F: 0, 187, 551, 1 870	PM: 1 390 PF: 1 540 F_1M: 1 760 F_1F: 1 870	PM: - PF: - F_1M: - F_1F: -	Parent: M/F: No toxicity was observed Offspring: No toxicity was observed (No effect on reproductive activity)
	Developmental toxicity study	0, 250, 500, 1 000	Dams: 1 000 Fetuses: 1 000	Dams: - Fetuses: -	Dams and fetuses: No toxicity was observed. (No teratogenicity)
Mouse	90-day subacute toxicity study	0, 1 500, 3 500, 7 000 ppm M: 0, 216, 521, 1 060 F: 0, 299, 644, 1 360	M: 1 060 F: 1 360	M: - F: -	M/F: No toxicity was observed
	18-month carcinogenicity study	0, 700, 2 000, 7 000 ppm M: 0, 82.2, 225, 820 F: 0, 103, 291, 1 010	M: 820 F: 1 010	M: - F: -	M/F: No toxicity was observed (No carcinogenicity)
Rabbit	Developmental toxicity study	0, 100, 250, 750	Dams: 250 Fetuses:750	Dams: 750 Fetuses: -	Dams: Miscarriage, decreased feed intake. Fetuses: No toxicity (No teratogenicity)

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
Dog	90-day subacute toxicity study	0, 100, 300, 1 000	M: 1 000 F: 1 000	M: - F: -	M/F: No toxicity was observed
	One-year chronic toxicity study	0, 100, 300, 1 000	M: 1 000 F: 1 000	M: - F: -	M/F: No toxicity was observed
ADI			NOAEL: 250 SF: 100 ADI: 2.5		
The critical study for setting ADI			Developmental toxicity study in rabbits.		

ADI: Acceptable Daily Intake, NOAEL: No-observed-adverse-effect level, SF: Safety factor
-: NOAEL or LOAEL could not be specified.
[1)]The adverse effect observed at LOAEL