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

Risk Assessment Report

Fenpicoxamid

(Pesticides)

Food Safety Commission of Japan (FSCJ)
May 2019

ABSTRACT

FSCJ conducted the risk assessment of a picoline amide fungicide, fenpicoxamid (CAS No. 517875-34-2), based on various documents.

The data used in the assessment include fate in animals (rats), livestock (goats and chicken), fate in plants (wheat and tomatoes), residues in plants, subacute toxicity (rats, mice and dogs), combined subacute toxicity/neurotoxicity (rats), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), genotoxicity, metabolism in vitro, and phototoxicity.

Major adverse effects of fenpicoxamid observed are suppressed body weight, increased organ weight and hepatocellular hypertrophy in the liver (mice), and dilatation of follicles in the thyroid (rats), and chronic progressive nephropathy (rats). Fenpicoxamid did not show neurotoxicity, carcinogenicity, reproductive toxicity, teratogenicity, and genotoxicity relevant to human health.

From the above results, fenpicoxamid (parent compound only) was identified as the relevant substance for the residue definition for dietary risk assessment in agricultural products and livestock products.
The lowest value of the no-observed adverse effect level (NOAEL) in all studies was 32.1 mg/kg bw/day in 18-month carcinogenicity study in mice. FSCJ specified an acceptable daily intake (ADI) of 0.32 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.
FSCJ considered it unnecessary to specify an acute reference dose (ARfD), since adverse effects which are likely elicited by a single oral administration of fenpicoxamid were not observed.

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

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
Rat	28-day subacute toxicity study	0, 2 300, 4 500, 9 000 ppm M: 0, 196, 395, 788 F: 0, 197, 377, 764	M: 788 F: 764	M: - F: -	M/F: No toxicity was observed
	90-day combined subacute toxicity/ neurotoxicity study	0, 3,000, 6 000, 11 500/14 000 ppm M: 0, 180, 365, 732 F: 0, 205, 413, 834	M: 732 F: 834	M: - F: -	M/F: No toxicity was observed (No subacute neurotoxicity)
	Two-year combined chronic toxicity/carcinogenicity study	0, 100, 300, 1 000 (mg/kg bw/day) M: 0, 101, 303, 1 010 F: 0, 101, 302, 1 010	M: - F: -	M: 101 F: 101	M/F: Multifocal or diffuse dilatation of follicles in the thyroid (No carcinogenicity)
	Two-generation reproductive toxicity study	0, 100, 300, 1 000 (mg/kg bw/day) PM : 0, 107, 322, 1 070 PF : 0, 105, 315, 1 050 F_1M : 0, 107, 322, 1 080 F_1F : 0, 106, 316, 1 050	Parent: PM: 1 070 PF: 1 050 F_1M: 1 080 F_1F: 1 050 Offspring: PM: 1 070 PF: 1 050 F_1M: 1 080 F_1F: 1 050	Parent: PM: - PF: - F_1M: - F_1F: - Offspring: PM : - PF : - F_1M : - F_1F : -	Parent: No toxicity was observed Offspring: No toxicity was observed (No effect on reproductive activity)
	Developmental toxicity study	0, 1 350, 4 050, 13 500 ppm 0, 103, 311, 1 040	Dams: 1 040 Fetuses: 1 040	Dams: - Fetuses: -	Dams and fetuses: No toxicity was observed. (No teratogenicity)
Mice	28-day subacute toxicity study	0, 1 500, 3 000, 6 000 ppm M: 0, 216, 444, 901 F: 0, 295, 652, 1 177	M: 444 F: 295	M: 901 F: 652	M/F: Increase in the absolute and relative weight of the adrenal gland.
	90-day subacute toxicity study	0, 300, 1 500, 3 000, 6 000/9 000 ppm M: 0, 39.6, 192, 399, 921 F: 0, 48.5, 303, 566, 1 110	M: 39.6 F: 48.5	M: 192 F: 303	M/F: Centrilobular hypertrophy of hepatocytes with eosinophilic changes in the cytoplasm

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
	18-month carcinogenicity study	0, 50, 300, 1 500, 3 000 ppm M: 0, 5.27, 32.1, 156 F: 0, 6.76, 39.7, 388	M: 32.1 F: 39.7	M: 156 F: 388	M/F: Centrilobular hypertrophy of hepatocytes with eosinophilic changes in the cytoplasm (No carcinogenicity)
Rabbit	Developmental toxicity study	0, 1 500, 5 000, 15 000 ppm 0, 52.8, 177, 495	Dams: 52.8 Fetuses: 495	Dams: 177 Fetuses: -	Dams: Decreased amount of feces Fetuses: No toxicity (No teratogenicity)
Dog	90-day subacute toxicity study	0, 3 000, 10 000, 30 000 ppm M: 0, 100, 408, 939 F: 0, 122, 353, 1 120	M: 939 F: 1 120	M: - F: -	M/F: No toxicity was observed
	One-year chronic toxicity study	0, 3 000, 10 000, 30 000 ppm M: 0, 84, 300, 981 F: 0, 80, 273, 1 010	M: 981 F: 1 010	M: - F: -	M/F: No toxicity was observed
ADI			NOAEL: 32.1 SF: 100 ADI: 0.32		
The critical study for setting ADI			18-month carcinogenicity study in mice		

-, NOAEL or LOAEL could not be specified.
[1)], The adverse effect observed at LOAEL