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

Risk Assessment Report

Fenpropathrin

(Pesticides)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted the risk assessment of a pyrethroid insecticide, fenpropathrin (CAS No. 39515-41-8), based on various documents.

The data used in the assessment include ; fate in animals (rats, goats and chicken), fate in plants (tomatoes and apples), residues in plants, acute neurotoxicity (rats), subacute toxicity (rats and dogs), subacute neurotoxicity (rats), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (mice and rats), three-generation reproduction toxicity (rats), developmental toxicity (rats and rabbits), developmental neurtotoxicity (rats), genotoxicity, immunotoxicity (rats), metabolic enzyme in the liver and *in vitro* effects on endocrine systems.

Major adverse effects of fenpropathrin observed are tremor and suppressed body weight. There was a gender difference in the effect on the nervous system (tremor) of rodents, where females were considered more sensitive for the effects than male. Fenpropathrin showed no carcinogenicity, reproductive toxicity, teratogenicity and genotoxicity.

From the above results, FSCJ identified the relevant substance for the residue definition for dietary risk assessment in agricultural products and livestock products to be fenpropathrin (parent compound only).

The lowest value of the no-observed-adverse-effect level (NOAEL) in all tests was 2.5 mg/kg bw/day based on the lowest-observed-adverse-effect level (LOAEL) of 12.5m /kg bw/d in the 2nd 90-day subacute toxicity study in male rats. Whilst, the finding at this LOAEL was only an increase in absolute and relative weight of the spleen. FSCJ recognized that a NOAEL of 19.5 mg/kg bw/day, which was higher than the LOAEL of 12.5 mg/kg bw/day, was obtained from male rats in a 1st combined two-year chronic toxicity/carcinogenicity study, a longer-term study compared to the 90-day study. Therefore, FSCJ judged that the NOAEL (2.5 mg/kg bw/day in the 2nd 90-day study) was not appropriate for a value to establish an acceptable daily intake (ADI). The next lowest NOAEL in all tests was obtained from a one-year chronic toxicity study in dogs. Consequently, FSCJ specified ADI of 0.027 mg/kg bw/day by applying a safety factor of 100 to the NOAEL of 2.79 mg/kg bw/day obtained in the one-year chronic toxicity study in dogs.

The lowest NOAEL for potential adverse effects of a single oral administration of fenpropathrin was 3.0 mg/kg bw/day obtained in the 2nd developmental toxicity study in rats. FSCJ specified an acute reference dose (ARfD) to be 0.03 mg/kg bw by applying a safety factor of 100 to the NOAEL.

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

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day) and Critical endpoints[1]
			FSCJ
Rat	90-day subacute toxicity study (the 1st study)	0, 15, 50, 150, 450, 600 ppm	M: 21.3 F: 25.2 M/F: Suppressed body weight, decreased feed consumption
		M: 0, 0.722, 2.49, 7.22, 21.3, 28.8 F: 0, 0.821, 2.82, 8.18, 25.2, 36.1	
	90-day subacute toxicity study (the 2nd study)	0, 2, 10, 50, 250 ppm	M: 2.5 F: 12.5 M/F: Increase in absolute and relative weight of the spleen
		M/F: 0, 0.1, 0.50, 2.5, 12.5	
	90-day subacute toxicity study (the 3rd study)	0, 3, 30, 100, 300, 600 ppm	Some evidence but inadequate quality to specify NOAEL. FSCJ considered relevant data as reference data.
		M/F: 0, 0.15, 1.5, 5, 15, 30	
	Comprehensive evaluation of 90-day subacute toxicity study (the 1st, 2nd and 3rd study)		
	90-day subacute neurotoxicity study	0, 60, 190, 570 ppm	M: 13 F: 5 M: Tremor F: Gait on toe and asthenic gait
		M: 0, 4, 13, 38. F: 0, 5, 15, 50	
	Combined two-year chronic toxicity/carcinogenicity study (the 1st study)	0, 50, 150, 450, 600 ppm	M: 19.5 F: 8.3 M/F: Increased mortality, generalized tremor (No carcinogenicity)
		M: 0, 2.2, 6.6, 19.5, 26.2 F: 0, 2.8, 8.3, 25.6, 40.8	
	Combined two-year chronic	0, 1, 5, 25, 125, 500 ppm	Some evidence but inadequate quality including no accordance with the current

[1] Major adverse effect observed at LOAEL

	toxicity/carcinogenicity study (the 2nd study)	M/F: 0.05, 0.25, 1.25, 6.25, 25	guideline on the number of animals examined to specify NOAEL. FSCJ regarded it as reference data.
	Comprehensive evaluation of Combined two-year chronic toxicity/carcinogenicity study (the 1st and 2nd study)		
	Three-generation reproductive toxicity study (the 1st study)	0, 40, 120, 360 ppm	Parent: PM: 7.8 PF: 3.1 F_1M: 9.2 F_1F: 3.5 F_2M: 9.3 F_2F: 3.6 Offspring: 3.1
		PM: 0,2.6, 7.8, 23.3 PF: 0, 3.1, 9.1, 27.7 F_1M: 0, 3.1, 9.2, 28.4 F_1F: 0, 3.5, 10.3, 34.7 F_2M: 0, 3.1, 9.3, 27.4 F_2F: 0, 3.6, 10.7, 733.1	Parent： M：Suppressed body weight F：Death, myospasm, irritable tremor Offspring：Death, generalized tremor (No effect on reproductive activity)
	Three-generation reproductive toxicity study (the 2nd study)	0, 5, 25, 250 ppm	Some evidence but FSCJ judged the 1st reproductive toxicity study where administered doses were higher than the 2nd one was adequate to specify the NOAEL for reproductive toxicity study. Therefore considered this study as reference data.
		0, 0.3, 1.7, 16.7	
	Comprehensive evaluation of three-generation reproductive activity study (the 1st study) and (the 2nd study)		
	Developmental toxicity study (the 1st study)	0, 0.4, 2.0, 10.0	Dams: 2.0 Fetuses: 10.0 Dams: Death, suppressed body weight Fetuses: No toxicity (No teratogenicity)
	Developmental toxicity study (the 2nd study)	0, 0.4, 1.5, 2.0, 3.0, 6.0, 10.0	Dams: 3.0 Fetuses: 10.0 Dams: Decreased body weight, suppressed body weight, decreased feed consumption Fetuses: No toxicity

			(No teratogenicity)
	Comprehensive evaluation of developmental toxicity study (the 1st and 2nd study)		Dams: 3.0 Fetuses: 10.0
	Developmental neurotoxicity study	0, 40, 100, 250 ppm --- Gestation period: 0, 3, 8, 19 Nursing period: 0, 7, 16, 40	Dams and offspring: Gestation period: 8, Nursing period: 16 Dams: Tremor, suppressed body weight Fetuses: Suppressed body weight (Lowering grip force of hind limb and changes in auditory startle reaction)
Mouse	Combined two-year chronic toxicity/carcinogenicity study	0, 40, 150, 600 ppm --- M: 0, 3.9, 13.7, 56.0 F: 0, 4.2, 16.2, 65.2	M: 56.0 F: 16.2 M: No toxicity F: Decreased RBC, Hb and Ht (No carcinogenicity)
Rabbit	Developmental toxicity study (the 1st study)	0, 4, 12, 36	Dams: 4 Fetuses: 36 Dams: Miscarriage , shivering tremor Fetuses: No toxicity (No teratogenicity)
	Developmental toxicity study (the 2nd study)	0, 1.5, 3, 6	Dams: 6 Fetuses: 6 Dams and Fetuses: No toxicity (No teratogenicity)
	Comprehensive evaluation of developmental toxicity study (the 1st and 2nd study)		
Dog	90-day subacute toxicity study	0, 250, 500, 1 000/750 ppm --- M: 0, 7.36, 15.5, 24.0 F: 0, 9.58, 15.9, 28.7	M/F: - M/F: Tremor

	One-year chronic toxicity study	0, 100, 250, 750 ppm M: 0, 2.92, 7.65, 23.2 F: 0, 2.79, 6.97, 23.4	M: 2.92 F: 2.79 M/F: Tremor
	Comprehensive evaluation of 90-day subacute toxicity study and one-year chronic toxicity study		
ADI			NOAEL: 2.79 SF: 100 ADI: 0.027
The critical study for setting ADI			One-year chronic toxicity study in dogs

ADI: Acceptable daily intake, NOAEL: No-observed-adverse-effect level, SF: Safety factor
-: NOAEL could not be specified, /: No description in relevant reference

Table 2. *Potential adverse effects of a single oral administration of fenpropathrin*

Species	Study	Dose (mg/kg bw and mg/kg bw/day)	Endpoints relevant to setting NOAEL and ARfD (mg/kg bw or mg/kg bw/day)[1]
Rat	Acute toxicity study	0, 5, 10, 20, 28, 40, 55, 75, 105	M/F: 5 M/F: Myospasm
		0, 25, 50, 90, 120, 160, 220, 300	M/F: 25 M/F: Myospasm
	Acute neurotoxicity study (the 1st study)	0, 3, 6, 15, 30	M: 15 F: 6 M/F: Tremor
	90-day subacute neurotoxicity study	0, 60, 190, 570 ppm M: 4, 13, 38 F: 5, 15, 50	M: 13 F: 15 M/F: Tremor
	Developmental toxicity study (the 2nd study)	0, 0.4, 1.5, 2.0, 3.0, 6.0, 10.0	Dams: 3.0 Suppressed body weight and decreased feed consumption
Mouse	Acute toxicity study	0, 1, 20, 26, 34, 44, 57, 75	M/F: 1 M/F: Myospasm, decresed locomotive activity
		0, 20, 50, 70, 90, 120, 170, 220	M/F: 20 M/F: Myospasm
Rabbit	Acute toxicity study	0, 89, 133, 200, 300, 450, 675、1 000	M/F: 89 M/F: Myospasm
Dog	Acute toxicity study	46, 100, 464, 1 000	M/F: 46 Tremor, salivation, vomiting
ARfD			NOAEL: 3.0 SF: 100 ARfD: 0.03
The critical study for setting ARfD			Developmental toxicity study (the 2nd study) in rats

ARfD, Acute reference dose; NOAEL, No-observed-adverse-effect level; SF, Safety factor

[1]The adverse effect observed at LOAEL