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

Risk Assessment Report

Cypermethrin

(Pesticides and Veterinary medicinal product)

Food Safety Commission of Japan (FSCJ)
February 2018

ABSTRACT

FSCJ conducted a risk assessment of cypermethrin (CAS No. 52315-07-8), a pyrethroid insecticide, based on various documents. FSCJ also evaluated alpha-cypermethrin and zeta-cypermethrin consisting of distinct ratio of 8 different optical isomers that compose cypermethrin using the reports of JMPR, the U.S.A. and other national authorities at the assessment.

The data used in the assessment include fate in animals (rats, mice and dogs), humans and livestocks (cattles, sheeps, chicken, rainbow trouts and trouts), fate in plants (cabbage and apples), residues in crops, subacute toxicity (rats, mice and dogs), subacute neurotoxicity (rats), chronic toxicity (dogs), combind chronic toxicity/carcinogenicity (rats and mice), carcinogenicity (rats), multigeneration reproductive toxicity (rats), developmental toxicity (rats and rabbits), genotoxicity and other effects on endocrine or neuronal systems.

Major adverse effects of cypermethrin, alpha-cypermethrin and zeta-cypermethrin observed are effects on nervous system (tremor etc.) and reduced body weight gain. FSCJ judged that these cypermethrins had no carcinogenicity, adverse effects on reproductivity, teratogenicity and genotoxicity relevant to human health. Based on the results from various studies, cypermethrin (parent compound including alpha- and zeta-cypermethrin) was identified as the residue definition for dietary risk assessment in agricultural and livestock products.

The lowest no-observed-adverse-effect level (NOAEL) obtained in all tests of cypermethrin, alpha- and zeta-cypermethrin was 2.25 mg/kg bw/day of alpha-cypermethrin in a 13-week subacute toxicity study in dogs. FSCJ specified an acceptable daily intake (ADI) of 0.022 mg/kg bw/day for cypermethrin including alpha- and zeta-cypermethrin, by applying a safety factor of 100 to the NOAEL.
The lowest NOAEL for potential adverse effects of single oral administration of cypermethrin, alpha- and zeta-cypermethrin was 4 mg/kg bw of alpha-cypermethrin obtained in an acute neurotoxicity study in rats. FSCJ specified the ARfD of 0.04 mg/kg bw for cypermethrin including alpha- and zeta-cypermethrin, by applying a safety factor of 100 to the NOAEL.

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

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day) and Critical endpoints[1]
Rats	5-week subacute toxicity study	0, 75, 150, 300, 1 500 ppm M: 6.8, 13.5, 27.3, 111 F: 9.5, 17.2, 30.3, 106	M: 13.5 F: 30.3 M: Increase of ALT F: Suppressed body weight
	90-day subacute toxicity study (the 1st study)	0, 50, 150, 500, 1 500ppm M: 0, 3.6, 10.8, 35.7, 95.8 F: 0, 5.7, 14.6, 49.1, 149	M: 10.8 F: 14.6 M: Increases in absolute and relative weight of the kidney F: Decreased Hb
	90-day subacute toxicity study (the 2nd study)	0, 150, 500, 1 500 ppm M: 11.8, 37.2, 116 F: 13.5, 45.0, 132	M: 37.2 F: 45.0 M/F: Suppressed body weight and decreased feed consumption
	90-day subacute toxicity study (the 3rd study)	0, 75, 150, 1 500 ppm M/F: 0, 3.75, 7.5, 75	M/F: 7.5 M/F: Suppressed body weight
	13-week subacute toxicity study	0, 25, 100, 400, 1 600 Unknown	M/F: 40 M/F: Suppressed body weight and decreased feed consumption
	91~95-day subacute toxicity study	0, 25, 100, 400, 1 600 ppm 0, Unknown, 5, 20, Unknown	M: 5 F: 20 M/F: Increase in relative weight of the liver
	90-day subacute neurotoxicity study (the 1st study)	0, 60, 300, 1 500 ppm M: 0, 4, 20, 100 F: 0, 5, 23, 111	M: 20 F: 23 M/F: Suppressed body weight

[1] Major adverse effect observed at LOAEL

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day) and Critical endpoints[1]
	90-day subacute neurotoxicity study (the 2nd study)	0, 75, 150, 1 500 ppm M/F : 0, Unknown, 15, 150	M/F: 15 M/F: Suppressed body weight and decreased feed consumption
	90-day sub-acute neurotoxicity study (the 3rd study)	0, 500, 1 300, 1 700 ppm M: 0, 31, 77, 102 F: 37, 95, 121	M: 31 F: 37 M/F: Suppressed body weight
	Two-year combined chronic toxicity/carcinogenicity study (the 1st study)	0, 1, 10, 100, 1 000 ppm M: 0, 0.0453, 0.463, 4.69, 47.1 F: 0, 0.0583, 0.588, 5.92, 60.3	M: 4.69 F: 5.92 M/F: Suppressed body weight and decreased feed consumption (No carcinogenicity was observed)
	Two-year combined chronic toxicity/carcinogenicity study (the 2nd study)	0, 20, 150, 1 000/1 500 ppm 0, 1, 7.5, 75	M/F: 7.5 M/F: Suppressed body weight (No carcinogenicity was observed)
	Three-generation reproductive toxicity study (the 1st study)	0, 10, 100, 500 ppm PM : 0, 0.99, 9.8, 49.7 PF : 0, 1.11, 11.0, 55.0 F_1M : 0, 1.08, 11.0, 55.0 F_1F : 0, 1.23, 12.3, 62.1 F_2M : 0, 1.05, 10.4, 50.9 F_2F : 0, 1.17, 11.8, 57.3	Parent and offspring PM: 9.8 PF: 11.0 F_1M: 11.0 F_1F: 12.3 F_2M: 10.4 F_2F: 11.8 Parent: Suppressed body weight and decreased feed consumption Offspring: Decrease in birth number, low body weight (No effect on reproductivity)

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day) and Critical endpoints[1]
	Three-generation reproductive toxicity study (the 2nd study)	0, 50, 150, 1 000/750 ppm 0, 3.8, 11, 56	Parent: 3.8 Offspring: 11 Parent: Suppressed body weight and decreased feed consumption Offspring: Suppressed body weight (No effect on reproductivity)
	Developmental toxicity study	0, 17.5, 35, 70	Parent: 17.5 Fetuses: 70 Dams: Suppressed body weight Fetuses: No toxic effect (No teratogenicity was observed)
Mice	97~101-week combined chronic toxicity/carcinogenicity study	0, 100, 400, 1 600 ppm M: 0, 7.08, 27.2, 128 F: 0, 8.33, 31.5, 139	M: 27.2 F: 31.5 M/F: Suppressed body weight (No carcinogenicity was observed)
Rabbits	Developmental toxicity study (the 1st study)	0, 3, 10, 30	Dams and fetuses: 30 Dams and fetuses: No toxic effect (No teratogenicity was observed)
	Developmental toxicity study (the 2nd study)	0, 100, 450, 700	Dams: 450 Fetuses: 700 Dams: Suppressed body weight Fetuses: No toxic effect (No teratogenicity was observed)
	Developmental toxicity study (the 3rd study)	0, 20, 50, 120	Dams and fetuses: 120 Dams and fetuses: No toxic effect (No teratogenicity was observed)
Dogs	90-day subacute toxicity study	0, 5, 50, 500, 1 500 ppm M：0, 0.152, 1.50, 15.2, 56.3 F：0, 0.196, 1.97, 21.0, 71.4	M: 15.2 F: 21.0 M/F: Diarrhea, tremor

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day) and Critical endpoints[1]
	Three-month subacute toxicity study	0, 300, 600, 800, 1 100 ppm M: 0, 10.4, 20.7, 24.6, 37.0 F: 0, 12.2, 25.4, 34.3, 45.2	M: 20.7 F: 25.4 M: Tremor F: Suppressed body weight
	12-month chronic toxicity study	0, 100, 200, 600, 1 100 M：0, 2.9, 6.0, 20.4, 33.9 F：3.3, 5.7, 18.1, 38.1	M: 6.0 F: 5.7 M: Abnormal walking F: Suppressed body weight
	52-week chronic toxicity study	M/F: 0, 1, 5, 15	M/F: 1 M/F: Gastrointestinal effects
	Two-year chronic toxicity study	0, 3, 30, 300, 600 pm	M: 9.16 F: 10.3 M/F: Suppressed body weight

[1] Major adverse effect observed at LOAEL