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Risk assessment

Cyclaniliprole (Pesticides)

Summary

Food Safety Commission of Japan

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of cyclaniliprole (CAS No. 1031756-98-5), an anthranilamide insecticide, based on results from various studies. Major treatment-related effects of cyclaniliprole were observed on liver (increased liver weight and increased alkaline phosphatase) in dogs and on thyroid (hypertrophy of follicular epithelial cells) in rats. None of neurotoxicity, carcinogenicity, reproductive toxicity, teratogenicity, immunotoxicity and genotoxicity were observed. Based on the results from various studies, only parent cyclaniliprole was identified as the relevant substance to the residue definition for dietary risk assessment in agricultural products. The lowest no-observed-adverse-effect level (NOAEL) obtained in all the toxicity studies was 1.29 mg/kg bw/day in a one-year chronic toxicity study in dogs. FSCJ has established an acceptable daily intake (ADI) of 0.012 mg/kg bw/day, by applying a safety factor of 100 to the NOAEL. FSCJ judged it unnecessary to specify an acute reference dose (ARfD) since no adverse effects, possibly elicited by a single oral administration, was observed.

Conclusion in Brief

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of cyclaniliprole (CAS No. 1031756-98-5), an anthranilamide insecticide, based on results from various studies.

The data used in the assessment include the fate in animals (rats, goats and chickens), fate in plants (apples and lettuce), residues in crops, subacute toxicity (rats, mice and dogs), subacute neurotoxicity (rats), chronic toxicity (rats and dogs), carcinogenicity (rats and mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), genotoxicity, and immunotoxicity (mice).

Major treatment-related effects of cyclaniliprole were observed on liver (increased liver weight and increased alkaline phosphatase) in dogs and on thyroid (hypertrophy of follicular epithelial cells) in rats. None of neurotoxicity, carcinogenicity, reproductive toxicity, teratogenicity, immunotoxicity and genotoxicity were observed.

Based on the results from various studies, only parent cyclaniliprole was identified as the relevant substance to the residue definition for dietary risk assessment in agricultural products.

The lowest no-observed-adverse-effect level (NOAEL) obtained in all the toxicity studies was 1.29 mg/kg bw/day in a one-year chronic toxicity study in dogs. FSCJ has established an acceptable daily intake (ADI) of 0.012 mg/kg bw/day, by applying a safety factor of 100 to the NOAEL.

FSCJ judged it unnecessary to specify an acute reference dose (ARfD), since no adverse effects, possibly elicited by a single oral administration, was observed.

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This is an English translation of excerpts from the original full report (October 2016-FS/640/2016). Only original Japanese texts have legal effects.
The original full report is available in Japanese at http://www.fsc.go.jp/fsciis/attachedFile/download?retrievalId=kya20160511024&fileId=201
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Levels relevant to toxicological evaluation of cyclaniliprole

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, 600, 6,000, 20,000 ppm M: 0, 39.9, 402, 1,330 F: 0, 43.3, 467, 1,590	M: 1,330 F: 1,590	M: - F: -	F/M: No toxicological effects
	90-day subacute neurotoxicity study	0, 600, 3,100, 16,000 ppm M: 0, 40, 204, 1,090 F: 0, 49, 240, 1,280	M: 1,090 F: 1,280	M: - F: -	F/M: No toxicological effects (Not neurotoxic)
	One-year chronic toxicity study	0, 200, 2,000, 6,000, 20,000 ppm M: 0, 9.21, 89.6, 277, 955 F: 0, 11.7, 117, 358, 1,210	M: 955 F: 1,210	M: - F: -	F/M: No toxicological effects
	Two-year carcinogenicity study	0, 200, 2,000, 6,000, 20,000 ppm M: 0, 7.93, 82.5, 249, 834 F: 0, 10.3, 103, 306, 1,040	M: 249 F: 1,040	M: 834 F: -	M: Hypertrophy of thyroid follicular epithelial cell F: No toxicological effects (Not carcinogenic)
	Two-generation reproductive toxicity study	0, 500, 3,000, 20,000 ppm PM: 0, 34.9, 207, 1,410 PF: 0, 39.2, 228, 1,590 F_1M: 0, 41.2, 245, 1,680 F_1F: 0, 45.6, 274, 1,840	Parent: PM: 1,410 PF: 1,590 F_1M: 1,680 F_1F: 1,840	Parent: PM: - PF: - F_1M: - F_1F: -	Parent F/M: No toxicological effects
			Offspring: PM: 1,410 PF: 1,590 F_1M: 1,680 F_1F: 1,840	Offspring: PM: - PF: - F_1M: - F_1F: -	Offspring F/M: No toxicological effects (No effect on reproduction)
	Developmental toxicity study	0, 100, 300, 1,000	Maternal: 1,000 Embryo/fetus: 1,000	Maternal: - Embryo/fetus: -	Maternal: No toxicological effects Embryo/fetus: No toxicological effects (Not teratogenic)
Mouse	90-day subacute toxicity study	0, 200, 1,200, 8,000 ppm M: 0, 27, 159, 1,020 F: 0, 34, 179, 1,350	M: 1,020 F: 1,350	M: - F: -	F/M: No toxicological effects
	18-month carcinogenicity study	0, 200, 1,250, 8,000 ppm M: 0, 22.7, 140, 884 F: 0, 31.6, 186, 1,320	M: 884 F: 1,320	M: - F: -	F/M: No toxicological effects (Not carcinogenic)
Rabbit	Developmental toxicity study	0, 100, 300, 1,000	Maternal: 1,000 Embryo/fetus: 1,000	Maternal: - Embryo/fetus: -	Maternal: No toxicological effects Embryo/fetus: No toxicological effects (Not teratogenic)
Dog	90-day subacute toxicity study	0, 100, 1,000, 10,000 ppm M: 0, 2.68, 26.8, 266 F: 0, 2.75, 26.9, 270	M: 2.68 F: 26.9	M: 26.8 F: 270	F/M: Increase in ALP
	One-year chronic toxicity study	0, 50, 150, 1,000, 10,000 ppm M: 0, 1.29, 4.07, 27.2, 259 F: 0, 1.47, 4.20, 27.6, 288	M: 1.29 F: 1.47	M: 4.07 F: 4.20	F/M: Increase in ALP
ADI			NOAEL: 1.29 SF: 100 ADI: 0.012		
The critical study for setting ADI			One-year chronic toxicity study in dogs		

M, Male; F, Female; F/M, both sexes; PM, Male in P (Parent) generation; PF, Female in P generation; F_1M, Male in F_1 generation; F_1F, Female in F_1 generation; -, LOAEL was not derived; [1)], The adverse effect observed at LOAEL; ADI, Acceptable daily intake; SF, Safety factor