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

Risk Assessment Report

Florpyrauxifen-benzyl

(Pesticides)

Food Safety Commission of Japan (FSCJ)

April 2019

ABSTRACT

FSCJ conducted the risk assessment of an allyl picolinic acid herbicide, Florpyrauxifen-benzyl (CAS No. 1390661-72-9), based on various documents.

The data used in the assessment include fate in animals (rats), livestock (goats and chicken), fate in plants (paddy rice), residues in crops, combined subacute toxicity/neurotoxicity (rats), subacute toxicity (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 data of florpyrauxifen-benzyl and its major metabolite in animals, metabolite A in critical toxicity studies for establish health based guidance values were submitted.

Only adverse effect of florpyrauxifen-benzyl observed was a slight suppression of body weight in 90-day oral toxicity study in female mice. Florpyrauxifen-benzyl showed no neurotoxicity, carcinogenicity, effects on reproductively, teratogenicity, genotoxicity and immunotoxicity.

From the above results, florpyrauxifen-benzyl and its metabolites A and B were identified as the relevant substances for the residue definition for dietary risk assessment in agricultural and livestock products.

The lowest value of the no-observed-adverse-effect level (NOAEL) in all tests was 240 mg/kg bw per day, the highest dose tested in 1-year toxicity study in dogs. The pesticide committee of FSCJ considered 1010 mg/kg bw/day, the highest dose tested in 90-day toxicity study is appropriate as the NOAEL for toxicity in dogs based on following reasons:

1. The blood concentration of florpyrauxifen-benzyl was not linear indicating the concentration is kinetically saturated at higher dose.
2. No increase in the blood concentration in 1-year study compared to that 90-day study indicated no accumulation of this compound in tissue/organ

In rats, the NOAELs of the combined 2-year chronic toxicity and carcinogenicity and the 2-generation reproductive toxicity studies were 303 and 309 mg//kg bw/day, both of the highest dose tested, respectively. The committee considered 1020 mg/kg bw per day is appropriate as the NOAEL for toxicity in rats based on the same interpretation as the dog studies.

In mice, body weight depression and decreased feed consumption were observed as toxicity in females at 1010 mg/kg bw per day in at 90-day toxicity study, however the changes observed were slight and the NOAEL for carcinogenicity study in mice was 803 mg/kg bw per day, the highest dose tested. Thus, the committee considered 803 mg/kg bw/day is appropriate as the NOAEL for toxicity in mice.

Based on the consideration mentioned above, the NOAEL in all tests was 803 mg/kg bw/day in an 18-month carcinogenicity study in mice. FSCJ specified an acceptable daily intake (ADI) of 8 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 florpyrauxifen-benzyl was observed, FSCJ concluded that an acute reference dose (ARfD) was not necessary to be specified.

Table 1. *Levels relevant to toxicological evaluation of florpyrauxifen-benzyl*

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
Rat	90-day combined subacute toxicity/neurotoxicity study	0, 100, 300, 1 000 M: 0, 104, 314, 1 060 F: 0, 101, 303, 1 020	M: 1 060 F: 1 020	M: - F: -	M/F: No toxic effect
	Two-year combined chronic toxicity/carcinogenicity study	0, 10, 50, 300 M: 0, 10.1, 50.6, 303 F: 0, 10.2, 50.8, 305	M: 303 F: 305	M: - F: -	M: No toxic effect (No carcinogenicity)
	Two-generation reproduction study	0, 10, 50, 300 PM: 0, 10.6, 53.1, 317 PF: 0, 10.3, 51.5, 309 F1 M: 0, 11.3, 56.6, 341 F1F: 0, 11.0, 55.6, 330	Parent PM: 317 PF:309 F1M:341 F1F:330 Offspring PM: 317 PF:309 F1M: 341 F1F: 330	Parent PM: - PF: - F1M: - F1F: - Offspring PM: - PF: - F1M: - F1F: -	Parent M/F: No toxic effect Offspring: No toxic effect (No effect on reporoductivity)
	Developmental toxicity study	0, 14 000 ppm 0, 975	Dams: 975 Fetuses: 975	Dams: - Fetuses: -	Dams and Fetuses: No toxic effect (No teratogenicity)
Mouse	90-day subacute toxicity study	0, 100, 300, 1 000 M: 0, 101, 304, 1 000 F: 0, 102, 303, 1 010	M: 1 000 F: 303	M: - F: 1 010	M: No toxic effect F: Suppressed body weight, decreased feed intake
	18-month carcinogenicity study	0, 50, 200, 800 (F), 1 000 (M) M: 0, 50.0, 200, 1 000 F: 0, 50.3, 201, 803	M: 1,000 F: 803	M: - F: -	M/F: No toxic effect (No carcinogenicity)
Rabbit	Developmental toxicity study	0, 27 000 ppm 0, 1 040	Dams: 1 040 Fetuses: 1 040	Dams: - Fetuses: -	Dams and fetuses: No toxic effect Fetuses: No toxic effect (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, 3 000, 10 000, 30 000 ppm M: 0, 106, 366, 1 010 F: 0, 115, 329, 1 220	M: 1 010 F: 1 220	M: - F: -	M/F: No toxic effect
	One-year chronic toxicity study	0, 300, 1 500, 9 000 ppm M: 0, 7.4, 37.7, 240 F: 0, 7.3, 44.6, 243	M: 240 F: 243	M: - F: -	M/F: No toxic effect
ADI			NOAEL: 803 SF: 100 ADI: 8		
The critical study for setting ADI			18-month carcinogenicity study in mice		

ADI: Acceptable Daily Intake, NOAEL: No observed adverse effect level, -: LOAEL could not be specified
[1)] : the adverse effect observed at LOAEL