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

Risk Assessment Report

Ametoctradin (2nd edition)

(Pesticides)

Food Safety Commission of Japan (FSCJ)
May 2019

ABSTRACT

FSCJ conducted the risk assessment of a pyrimidilamine insecticide, ametoctradin (CAS No. 865318-97-4), based on various documents. The documents used in this assessment included newly presented data on ADME (goats and chicken), residues in crops (soybean and adzuki bean) and residues in livestock products (cattle).

The data used in the assessment include fate in animals (rats, goats and chicken), fate in plants (tomato and potato), residues in plants, subacute toxicity (rats, mice and dogs), subacute neurotoxicity (rats), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproduction (rats), developmental toxicity (rats and rabbits), genotoxicity and immunotoxicity.

Major adverse effect of ametoctradin observed was only suppressed body weight in dogs. Ametoctradin showed none of neurotoxicity, carcinogenicity, effects on reporoductivity, teratogenicity, genotoxicity and immunotoxicity.
From the above results, ametoctradin (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 tests was 273 mg/kg bw/day in a one-year chronic toxicity study in dogs. FSCJ specified an acceptable daily intake (ADI) of 2.7 mg/kg bw/day[1] by applying a safety factor of 100 to the NOAEL.
Since the absence of any toxicological effects that would be likely to be elicited by a single dose of ametoctradin was observed, FSCJ considered it was unnecessary to specify the ARfD.

[1] The ADI was the same as the previous ADI (FSCJ, 2013 January)

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

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, 1 500, 5 000, 15 000 ppm M: 0, 106, 358, 1 080 F: 0, 123, 416, 1 240	M: 1 080 F: 1 240	M: - F: -	M/F: No toxicity was observed.
	90-day subacute neurotoxicity study	0, 1 500, 5 000, 15 000 ppm M: 0, 89.4, 300, 921 F: 0, 105, 350, 1 080	M: 921 F: 1 080	M: - F: -	M/F: No toxicity was observed. (No neurotoxicity)
	Two-year combined chronic toxicity/carcinogenicity study	0, 150, 1 500, 15 000* ppm M: 0, 6.9, 69.9, 871 F: 0, 9.6, 95.0, 979	M: 871 F: 979	M: - F: -	M/F: No toxicity was observed (No carcinogenicity)
	Two-generation reproductive activity study	0, 100, 300, 1 000 PM : 0, 94.4, 283, 944 PF : 0, 95.5, 285, 951 F_1M : 0, 93.6, 280, 939 F_1F : 0, 96.8, 291, 965	Parent and offspring PM: 944 PF: 951 F_1M: 939 F_1F: 965	Parent and offspring PM: - PF: - F_1M: - F_1F: -	Parent and offspring: No toxicity was observed (No effect on reproductive activity)
	Developmental toxicity study	0, 100, 300, 1 000	Dams: 1 000 Fetuses: 1 000	Dams: - Fetuses: -	Dams and fetuses: No toxicity was observed. (No teratogenicity)
Mice	90-day sub-acute toxicity study	0, 500, 2 000, 6 000 ppm M: 0, 101, 370, 1 120 F: 0, 168, 597, 2 090	M: 1 120 F: 2 090	M: - F: -	M/F: No toxicity was observed
	18-month carcinogenicity study	0, 60, 600, 6 000 ppm M: 0, 10.6, 104, 1 100 F: 0, 15.2, 154, 1 540	M: 1 000 F: 1 540	M: - F: -	M/F: No toxicity was observed (No carcinogenicity)

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
Rabbits	Developmental toxicity study	0, 100, 300, 1 000	Dams: 1 000 Fetuses: 1 000	Dams: - Fetuses: -	Dams and Fetuses: No toxicity was observed (No teratogenicity)
Dogs	90-day subacute toxicity study	0, 3 000, 10 000, 30 000 ppm M: 0, 93, 299, 912 F: 0, 100, 330, 1 010	M: 1 000 F: 1 000	M: - F: -	M/F: No toxicity was observed
	One-year chronic toxicity study	0, 3 000, 10 000, 30 000 ppm M: 0, 84, 273, 848 F: 0, 85, 305, 936	M: 273 F: 305	M: 848 F: 936	M/F: Suppressed body weight
ADI			NOAEL: 273 SF: 100 ADI: 2.7		
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 or LOAEL could not be specified.
[1)] The adverse effect observed at LOAEL