

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

Risk Assessment Report

Aminocyclopyrachlor

(Pesticides)

Food Safety Commission of Japan (FSCJ)
May 2017

ABSTRACT

FSCJ conducted a risk assessment of aminocyclopyrachlor (CAS No. 858956-08-8), a pyridine carboxylic acid herbicides, based on results from various studies.

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

The major adverse effect of aminocyclopyrachlor was suppressed body weight in rats. Aminocyclopyrachlor has no neurotoxicity, carcinogenicity, reproductive toxicity, teratogenicity, immunotoxicity and genotoxicity.

Based on various studies, aminocyclopyrachlor (parent compound only) was identified as the residue definition for dietary risk assessment in livestock products.

The lowest no-observed-effect level (NOAEL) obtained in all studies was 91.9 mg/kg bw/day in a two-generation reproductive toxicity study in rats. FSCJ specified an acceptable (ADI) of 0.91 mg/kg bw/day, applying a safety factor of 100 to the NOAEL.

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

Levels relevant to toxicological evaluation of aminocyclopyrachlor

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, 2,000, 6,000, 18 000 ppm	M: 349 F: 448	M: 1 050 F: 1 430	FM: Suppressed body weight (No subacute neurotoxicity)
		M: 0, 35, 114, 349, 1 050 F: 0, 45, 146, 448, 1 430			
	Two-year combined chronic toxicity/carcinogenicity study	0, 600, 2,000, 6,000, 18 000 ppm	M: 279 F: 309	M: 892 F: 957	FM: Suppressed body weight
		M: 0, 27.4, 97.1, 279, 892 F: 0, 29.3, 99.8, 309, 957			
Two-generation reproductive toxicity study	0, 500, 1 500, 5 000, 17 000 ppm	Parent PM: 91.9 PF: 367 F ₁ M: 126 F ₁ F: 465	Parent PM: 299 PF: 1 240 F ₁ M: 426 F ₁ F: 1 670	Parent M: Suppressed body weight F: Suppressed body weight and hypertrophy of thyroid follicular cell	
	F ₁ M: 0, 42.3, 126, 426, 1 520 F ₁ F: 0, 46.2, 105, 465, 1 670	Offspring PM: 299 PF: 367 F ₁ M: 426 F ₁ F: 465	Offspring PM: 1 050 PF: 1 240 F ₁ M: 1 520 F ₁ F: 1 670	Offspring FM: Suppressed body weight (No adverse effect on fertility)	
	Developmental toxicity study	0, 30, 100, 300, 1 000	Maternal: 1 000 Embryo/fetus: 1 000	Maternal: - Embryo/fetus: -	Maternal: No toxicity Embryo/fetus: No toxicity (Not teratogenic)
Mouse	90-day subacute toxicity study	0, 300, 1 000, 3 000, 7 000 ppm M: 0, 46.8, 154, 459, 1 090	M: 1 090 F: 1 620	M: - F: -	FM: No toxicity

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints ¹⁾
		F: 0, 60.7, 230, 649, 1 620			
	18-month carcinogenicity study	0, 300, 1 000, 3 000, 7 000 ppm M: 0, 38.7, 133, 393, 876 F: 0, 49.9, 171, 527, 1 190	M: 876 F: 1 190	M: - F: -	FM: No toxicity (Not carcinogenic)
Rabbit	Developmental toxicity study	0, 100, 300, 500, 1 000	Maternal: 300 Embryo/fetus: 1 000	Maternal: 500 Embryo/fetus: -	Maternal: Soft stools, etc. Embryo/fetus: No toxicity (Not teratogenic)
	90-day subacute toxicity study	0, 250, 1 250, 5 000, 15 000 M: 0, 6.46, 33.3, 126, 426 F: 0, 7.02, 37.9, 124, 388	M: 426 F: 388	M: - F: -	FM: No toxicity
Dog	One-year chronic toxicity study	0, 1 250, 5 000, 15 000, 30 000 M: 0, 37.9, 178, 465, 1 080 F: 0, 46.9, 175, 542, 1 070	M: 1 080 F: 1 070	M: - F: -	FM: No toxicity
ADI			NOAEL: 91.9 SF: 100 ADI: 0.91		
The critical study for setting ADI			Two-generation reproductive toxicity study in rats		

ADI, Acceptable daily intake; SF, Safety factor; NOAEL, No observed adverse effect level; -, NOAEL or LOAEL could not be specified

¹⁾, The adverse effect observed at LOAEL