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

Risk Assessment Report

Dicloromezotiaz

(Pesticides)

Food Safety Commission of Japan (FSCJ)
April 2023

ABSTRACT

The FSCJ conducted a risk assessment of dicloromezotiaz (CAS No.1263629-39-5), a mesoionic insecticide, based on various documents.

The data used in the assessment include fate in plants (including Japanese radish and lettuce), residues in crops, fate in animals (rats), combined subacute toxicity/neurotoxicity (rats), subacute toxicity (rats, mice and dogs), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), acute neurotoxicity (rats), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits) and genotoxicity.

The major adverse effect of dicloromezotiaz was observed in body weight (suppressed weight gain). No effects were observed for neurotoxicity, fertility, teratogenicity or genotoxicity.

Although an increase in astrocytoma (malignant) and testicular interstitial cell tumor were observed in male rats in a two-year combined chronic toxicity/carcinogenicity study, the likelihood of a genotoxic mode of action for tumor formation was minimal, thus it was considered possible to specify a threshold dose for the assessment.

Based on these results, dicloromezotiaz (parent compound only) was identified as the relevant substance for the residue definition for dietary risk assessment in agricultural products.

The lowest no-observed-adverse-effect level (NOAEL) obtained from these studies was 122 mg/kg bw per day in a two-generation reproductive toxicity study in rats. FSCJ specified an acceptable daily intake (ADI) of 1.2 mg/kg bw per day based on the NOAEL after applying a safety factor of 100.

Since there was no adverse effect likely to be elicited by a single oral administration of dicloromezotiaz, the FSCJ considered it unnecessary to specify an acute reference dose (ARfD).

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

Species	Study	Dose (mg/kg bw/ per day)	NOAEL (mg/kg bw per day)	LOAEL (mg/kg bw per day)	Critical endpoints[1)]
Rat	28-day subacute toxicity study	0, 600, 2 000, 6 000, 12 000 ppm M: 0, 45.2, 147, 446, 902 F: 0, 46.0, 152, 439, 902	M: 902 F: 902	M: - F: -	M/F: No toxicity
	90-day combined subacute toxicity/ neurotoxicity study	0, 600, 2 000, 6 000, 20 000 ppm M: 0, 32.1, 110, 330, 1 110 F: 0, 40.8, 135, 393, 1 330	M: 330 F: 393	M: 1 110 F: 1 330	M/F: Vacuolation of zona fasciculata of the adrenal cortex (No subacute neurotoxicity is observed.)
	Two-year combined chronic toxicity/ carcinogenicity study	0, 600, 2 000, 6 000, 20 000 ppm M: 0, 31.8, 103, 321, 1 070 F: 0, 33.1, 112, 347, 1 150	M: 321 F: 1 150	M: 1070 F: -	M: Increased incidence of astrocytoma (malignant), Interstitial cell tumor of testis F: No toxicity
	Two-generation reproductive toxicity study	0, 100, 300, 2 000, 15 000 ppm PM: 0, 6.01, 18.3, 122, 925 PF: 0, 7.02, 21.7, 145, 1 070 F_1M: 0, 7.17, 21.6, 148, 1 120 F_1F: 0, 8.05, 24.7, 172, 1 270	Parent PM: 122 PF: 145 F_1M: 148 F_1F: 172 Offspring PM: 122 PF: 145 F_1M: 148 F_1F: 172	Parent PM: 925 PF: 1 070 F_1M: 1 120 F_1F: 1 270 Offspring PM: 925 PF: 1 070 F_1M: 1 120 F_1F: 1 270	Parent: Suppressed body weight gain, etc. Offspring: Suppressed body weight gain, etc. (No effect on fertility is observed.)
	Developmental toxicity study	0, 100, 300, 1 000	Dams: 1 000 Fetuses: 1 000	Dams: - Fetuses: -	Dams: No toxicity Fetuses: No toxicity (No teratogenicity observed.)
Mouse	90-day subacute toxicity study	0, 300, 1 000, 3 000, 7 000 ppm M: 0, 47.2, 150, 469, 1 130 F: 0, 63.0, 212, 657, 1 500	M: 1 130 F: 1 500	M: - F: -	M: No toxicity
	18-month carcinogenicity study	0, 300, 1 000, 3 000, 7 000 ppm M: 0, 40.6, 134, 404, 948 F: 0, 49.0, 159, 495, 1 140	M: 948 F: 1 140	M: - F: -	M/F: No toxicity (No carcinogenicity is observed.)

Rabbit	Developmental toxicity study	0, 100, 300, 1 000	Dams: 1 000 Fetuses:1 000	Dams: - Fetuses: -	Dams: No toxicity Fetuses: No toxicity (No teratogenicity is observed.)
Dog	90-day subacute toxicity study	0, 1 000, 3 000, 10 000, 30 000 ppm M: 0, 35.5, 110, 353, 1 160 F: 0, 42.5, 109, 388, 1 210	M: 1 160 F: 1 210	M: - F: -	M/F: No toxicity
	One-year chronic toxicity study	0, 1 250, 5 000, 15 000, 30 000 ppm M: 0, 41.7, 175, 551, 937 F: 0, 43.0, 183, 498, 972	M: 937 F: 972	M: - F: -	M/F: No toxicity
ADI			NOAEL: 122 SF: 100 ADI: 1.2		
The critical study for setting ADI			Two-generation reproductive toxicity study (rat)		

ADI, Acceptable daily intake; NOAEL, No-observed-adverse-effect level; SF, Safety factor
[1)] The adverse effect observed at LOAEL
-: LOAEL could not be specified.