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

Risk Assessment Report

Thiencarbazone-methyl

(Pesticides)

Food Safety Commission of Japan (FSCJ)
October 2020

ABSTRACT

FSCJ conducted the risk assessment of a sulfonylaminocarbonyl-triazolinone herbicide, thiencarbazone-methyl (CAS No. 317815-83-1), based on various documents.

The data used in the assessment include fate in animals (rats, goats and chicken), fate in plants (wheat and sugar beet), residues in plants, subacute toxicity (rats, mice and dogs), subacute toxicity (rats), chronic toxicity (dogs), combined acute toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), and genotoxicity.

Major adverse effects of thiencarbazone-methyl observed are crystal formation in the urinary tract, and related changes in the kidney (dilation of the renal pelvis in rats and mice) and the urinary bladder (stones, inframation, and transitional epithelialcell hyperplasia). Thiencarbazone-methyl showed no effects on reproduction, no teratogenicity and genotoxicity.

In a 78-week carcinogenicity study in mice, treatment-related increases in transitional cell papillomas in the urinary bladder in both male and female, transitional cell carcinoma in the prostatic urethra in male, and transitional cell carcinomas in the urinary bladder in female were observed. However, a genotoxic mechanism was unlikely involved in tumor induction, and FSCJ considered it possible to establish a threshold dose in the assessment.

FSCJ identified thiencarbazone-methyl (parent compound only) 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 117 mg/kg bw/day in a one-year chronic toxicity study in dogs. FSCJ specified an acceptable daily intake (ADI) of 1.1 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.
The lowest NOAEL for potential adverse effects of a single oral administration of thiencarbazone-methyl was 512 mg/kg bw/day obtained in acute neurotoxicity studies in rats. FSCJ considered it unnecessary to specify an acute reference dose (ARfD), since the NOAEL was above the cut-off level (500 mg/kg bw).

Table 1. *Levels relevant to toxicological evaluation of thiencarbazone-methyl*

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, 400, 2 000, 7 000 ppm M: 0, 24.7, 123, 439 F: 0, 30.8, 154, 543	M: 123 F: 154	M: 439 F: 543	M/F : Renal pelvis stone, transitional cell hyperplasia of the renal collecting duct and urinary bladder
	90-day subacute neurotoxicity study	0, 500, 2 000, 6 000 ppm M: 0, 33.1, 137, 411 F: 0, 42.4, 171, 527	M: 411 F: 527	M: - F: -	M/F: No toxicity was observed. (No subacute neurotoxicity)
	Combined two-year chronic toxicity/carcinogenicity study	Chronic toxicity group: 0, 200, 500, 2 500, 5 000 ppm Carcinogenicity group: 0, 500, 2 500, 5 000 ppm Chronic toxicity group: M: 0, 10.6, 27.2, 136, 269 F: 0, 13.2, 35.8, 177, 367 Carcinogenicity group: M: 0, 22.8, 115, 234 F: 0, 29.9, 153, 313	M: 234 F: 313	M: - F: -	M/F: No toxicity was observed. (No carcinogenicity)
	Two-generation reproductive toxicity study	0, 500, 2 500, 10 000 ppm PM: 0, 46.0, 245, 946 PF: 0, 55.6, 264, 968 F_1M: 0, 50.2, 261, 992 F_1F: 0, 68.0, 353, 1 280	Parent and offspring: PM: 245 PF: 264 F_1M: 261 F_1F: 353	Parent and offspring: PM: 946 PF: 968 F_1M: 992 F_1F: 1 280	Parent: M/F: Kidney stones, submucosal edema in the urinary bladder, transitional cell hyperplasia in the urinary bladder Offspring: Kidney stones and bladder stones (No effect on reproductive activity)
	Developmental toxicity study	0, 50, 200, 1 000	Dams: 200 Fetuses: 200	Dams: 1 000 Fetuses: 1 000	Dams: Suppressed body weight, decreased feed intake Fetuses: Low body weight, delayed ossification (No teratogenicity)

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
Mouse	90-day subacute toxicity study	0, 500, 2 000, 4 000 ppm M: 0, 76, 315, 637 F: 0, 103, 409, 789	M: 315 F: 789	M: 637 F: -	M: Bladder stones, submucosal inflammatory cell infiltration, transitional cell diffuse inflammation and diffuse hyperplasia, in the bladder. F: No toxicity was observed.
	78-week carcinogenicity study	0, 200, 1 000, 4 000 ppm M: 0, 29.2, 147, 599 F: 0, 36.8, 185, 758	M: 147 F: 185	M: 599 F: 758	M/F: Bladder stones, transitional cell hyperplasia in the urinary bladder. (M/F: Transitional cell papillomas in the urinary bladder. M: transitional cell carcinoma in the prostatic urethra. F: transitional cell carcinoma in the bladder.)
Rabbit	Developmental toxicity study	0, 50, 125, 500	Dams: 125 Fetuses: 125	Dams: 500 Fetuses: 500	Dams: Decreased/Suppressed body weight, decreased feed intake Fetuses: Low body weight (No teratogenicity)
Dog	90-day subacute toxicity study	0, 1 000, 5 000, 10 000 ppm M: 0, 34, 149, 335 F: 0, 32, 159, 351	M: 149 F: 159	M: 335 F: 351	M/F: Urinary bladder hemorrhage, transitional cell hyperplasia in the urinary bladder
	One-year chronic toxicity study	M: 0, 1 000, 4 000, 8 000/7 000/6 000 ppm F: 0, 1 000, 4 000, 8 000/7 000 ppm M: 0, 29, 117, 179 F: 0, 27, 127, 200	M: 117 F: 200	M: 179 F: -	M: Bladder stones, inflammation of the bladder, transitional cell hyperplasia in the urinary bladder F: No toxicity was observed
ADI			NOAEL: 117 SF: 100 ADI: 1.1		
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
-: LOAEL could not be specified.
[1)]The adverse effect observed at LOAEL

Table 2. *Potential adverse effects of a single oral administration of thiencarbazone-methyl*

Species	Study	Dose (mg/kg bw)	Endpoints relevant to setting NOAEL and ARfD (mg/kg bw or mg/kg bw/day) [1)]
Rat	Acute neurotoxicity study	0, 131, 512, 2 180	M/F: 512 Urine stains on the hair around the external genitalia, decreased locomotive activity and decreased locomotion
ARfD			Specification not required. (Above the cut off value (500 mg/kg bw))

ARfD, Acute reference dose

1) The adverse effect observed at LOAEL