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

Risk Assessment Report

Pencycuron (Second edition)

(Pesticides)

Food Safety Commission of Japan (FSCJ)
October 2021

ABSTRACT

The FSCJ conducted a risk assessment of pencycuron (CAS No. 66063-05-6), a urea fungicide, based on submitted documents. For this second edition, additional test results were submitted by the Ministry of Health, Labour and Welfare, including fate in animals (goats and chickens), residue in livestock products (cattle and chickens), developmental toxicity (rats) and reverse mutation using bacteria.

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

Major adverse effects of pencycron were observed in the liver (including organ weight gain and hepatocellular hypertrophy in rats and mice). No neurotoxicity, carcinogenicity, effects on fertility, teratogenicity or genotoxicity was observed.

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

Among the no-observed-adverse-effect levels (NOAELs) obtained from various studies, the lowest value was 3.2 mg/kg bw per day in the P males of the two-generation reproductive toxicity study (the 1st study) using rats. However, considering the results of the two-generation reproductive toxicity study (the 2nd study) in conjunction with the 1st study, a comprehensive evaluation of the NOAEL for rats determined that the value of 5.3 mg/kg bw per day in the F2 males of the 2nd study is more appropriate to be regarded as the lowest NOAEL for toxicity studies conducted with rats.

The FSCJ specified an acceptable daily intake (ADI) of 0.053 mg/kg bw per day by applying a safety factor of 100 to the NOAEL of 5.3 mg/kg bw per day from the aforementioned two-generation reproductive toxicity study in rats.

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

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

Species	Study	Dose (mg/kg bw per day)	NOAEL (mg/kg bw per day) [1)]
Rat	14-week subacute toxicity study	0, 80, 400, 2 000, 10 000 ppm M: 0, 4.62, 23.9, 120, 610 F: 0, 5.57, 27.5, 138, 712	M: 120 F: 27.5 M: Increased absolute and relative weights of the liver, etc. F: Suppressed body weight gain
	90-day subacute neurotoxicity study	0, 500, 2 500, 15 000 M: 0, 34.9, 181, 1 170 F: 0, 51.2, 275, 1 840	M: 1 170 F: 275 M: No toxicity F: Demarcation of the hepatic lobular structure (No subacute neurotoxicity is observed.)
	Combined two-year chronic toxicity/carcinogenicity study	0, 50, 500, 5 000 ppm M: 0, 1.79, 18.4, 186 F: 0, 2.20, 21.9, 229	M: 18.4 F: 21.9 M/F: Suppressed body weight gain, etc. (No carcinogenicity is observed.)
	Two-generation reproductive toxicity study (the 1st study)	0, 50, 500, 10 000 ppm PM: 0, 3.2, 32.7, 676 PF: 0, 4.6, 48.7, 998 F_1M: 0, 3.4, 34.0, 704 F_1F: 0, 4.9, 48.7, 1 000	Parent and offspring PM: 3.2 PF: 4.6 F_1M: 3.4 F_1F: 4.9 Parent: Suppressed body weight gain, etc. Offspring: Suppressed body weight gain (No effect on fertility is observed.)
	Two-generation reproductive toxicity study (the 2nd study)	0, 100, 1 000, 10 000 ppm PM: 0, 5.8, 58.4, 596 PF: 0, 6.7, 70.8, 739 F_1M: 0, 6.9, 71.7, 746 F_1F: 0, 8.0, 87.6, 911 F_2M: 0, 5.3, 56.5, 573 F_2F: 0, 6.9, 69.9, 722	Parent: PM: 5.8 PF: 6.7 F_1M: 6.9 F_1F: 8.0 F_2M: 5.3 F_2F: 6.9 Offspring: PM: 58.4 PF: 70.8 F_1M: 71.7 F_1F: 87.6

Species	Study	Dose (mg/kg bw per day)	NOAEL (mg/kg bw per day) [1)]
			Parent: Increased liver weights, etc. Offspring: Suppressed body weight gain (No effect on fertility is observed.)
	Developmental toxicity study (the 1st study)	0, 40, 200, 1 000	Dams and Fetuses: 1 000 Dams and Fetuses: No toxicity (No teratogenicity is observed.)
Mouse	90-day subacute toxicity study	0, 80, 400, 2 000, 10 000 ppm M: 0, 9.7, 50.0, 264, 1 340 F: 0, 12.6, 64.7, 315, 1 550	M: 50.0 F: 315 M: Increased LDH and ALT levels F: Increased relative liver weights, etc.
	Two-year combined chronic toxicity/carcinogenicity study	0, 50, 500, 5 000 ppm M: 0, 4.42, 42.9, 468 F: 0, 4.23, 44.4, 465	M: 42.9 F: 465 M: Suppressed body weight gain, Diffuse hepatocellular hypertrophy and degeneration F: No toxicity (No carcinogenicity is observed.)
Rabbit	Developmental toxicity study	0, 200, 600, 2 000	Dams and Fetuses: 2 000 Dams and Fetuses: No toxicity (No teratogenicity is observed.)
Dog	One-year chronic toxicity study	0, 100, 1 000, 10 000 M: 0, 3.15, 32.9, 324 F: 0, 3.23, 33.9, 355	M: 324 F: 355 M/F: No toxicity
ADI			NOAEL: 5.3 SF: 100 ADI: 0.053
The critical study for setting ADI			The 1st and 2nd two-generation reproductive toxicity studies (rat)

ADI, Acceptable daily intake; ALT, Alanine transaminase; LDH, Lactate dehydrogenase; NOAEL, No-observed-adverse-effect level; SF, Safety factor

[1)] The adverse effect observed at LOAEL.