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

Risk Assessment Report

Tiadinil (2nd Edition)

(Pesticides)

Food Safety Commission of Japan (FSCJ)

September 2020

ABSTRACT

FSCJ conducted the risk assessment of a thiadiazolecarboxamide insecticide, tiadinil (CAS No. 223580-51-6), based on various documents. Data on fate in animals (goats and chicken) and residue in livestock products (lactating caw and laying hen) were newly available in this assessment.

The data used in the assessment include fate in animals (rats, goats and chicken), fate in plants (paddy rice), residues in crops, acute toxicity (rats and rabbits), subacute toxicity (rats and dogs), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproduction toxicity (rats), developmental toxicity (rats and rabbits), genotoxicity and mechanism of liver tumor induction in mice.

Major adverse effects of tiadinil observed are increased organ weight and liver hypertrophy, and vacuolation of renal tubular epithelial cells in the kidney. Tiadinil showed no effects on reproduction, teratogenicity and genotoxicity relevant to human health.
In a carcinogenicity study in mice, an increased incidence of hepatocellular adenomas was observed. However, a genotoxic mechanism was unlikely involved in tumor induction, and it was considered possible to establish a threshold dose in the assessment.
FSCJ identified the relevant substances for the residue definition for dietary risk assessment in agricultural products to be tiadinil and its metabolite D and E, for that in livestock products to be tiadinil and its metabolite C, and for that in livestock products and that for fishery products to be tiadinil (parent substance only).

The lowest value of the no-observed-adverse-effect level (NOAEL) in all tests was 4 mg/kg bw/day in a one-year chronic toxicity study in dogs. FSCJ specified an acceptable daily intake (ADI) of 0.04 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 tiadinil was 150 mg/kg bw/day obtained in developmental toxicity studies in rats and in rabbits. FSCJ specified an acute reference dose (ARfD) to be 1.5 mg/kg bw by applying a safety factor of 100 to the NOAEL.

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

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)[1]	
			FSCJ	Reference (Summary reports)
Rat	90-day subacute toxicity study	0, 80, 400, 2 000, 5 000 ppm M: 0, 6.06, 28.0, 139, 359 F: 0, 6.36, 32.8, 157, 411	M: 28.0 F: 6.36 M: Increased relative weight of the liver F: Increased relative and absolute weight of the liver	M: 28.0 F: 6.36 M: Increased relative weight of the liver F: Increased relative and absolute weight of the liver
	90-day subacute neurotoxicity study	0, 400, 2 000, 5 000 ppm M: 0, 27, 139, 355 F: 0, 29, 146, 360	M: 139 F: 146 M/F: Suppressed body weight (No subacute neurotoxicity was observed)	M: 139 F: 146 M/F: Suppressed body weight (No subacute neurotoxicity was observed)
	Two-year combined chronic toxicity/carcinogenicity study	0, 80, 400, 2 000 ppm M: 0, 3.67, 19.0, 95.2 F: 0, 4.57, 23.2, 115	M: 19.0 F: 23.2 M/F: Suppressed body weight (No carcinogenicity)	M: 19.0 F: 23.2 M/F: Suppressed body weight (No carcinogenicity)
	Two-generation reproductive toxicity study	0, 80, 600, 5 000 ppm PM: 0, 4.90, 36.4, 300 PF: 0, 7.15, 53.6, 448 F_1M: 0, 5.63, 42.2, 353 F_1F: 0, 7.72, 58.4, 489	Parent and offspring PM: 36.4 PF: 53.6 F_1M: 42.2 F_1F: 58.4 Parent and offspring Suppressed body weight (No effects on reproductive activity)	Parent and offspring PM: 36.4 PF: 53.6 F_1M: 42.2 F_1F: 58.4 Parent and offspring Suppressed body weight (No effects on reproductive activity)
	Developmental toxicity study	0, 30, 150, 750	Dams: 150 Fetuses: 750 Dams: Decreased /suppressed body weight Fetuses: No toxicity was observed. (No teratogenicity)	Dams: 150 Fetuses: 750 Dams: Suppressed body weight Fetuses: No toxicity was observed. (No teratogenicity)
Mouse	18-month carcinogenicity study	0, 150, 1 000, 7 000 ppm	M: 196 F: 267	M: 196 F: 267

		M: 0, 29.0, 196, 1 310 F: 0, 40.0, 267, 1 790	M/F: Increased incidence of hepatocellular adenomas	M/F: Increased incidence of hepatocellular adenomas
Rabbit	Developmental toxicity study	0, 30, 150, 600	Dams: 150 Fetuses: 600 Dams: Decreased/suppressed body weight Fetuses: No toxicity was observed (No teratogenicity was observed)	Dams: 150 Fetuses: 600 Dams: Decreased/suppressed body weight Fetuses: No toxicity was observed (No teratogenicity was observed)
Dog	90-day subacute toxicity study	0, 20, 100, 500	M/F: 20 M/F: Centrilobular hypertrophy of hepatocytes	M/F: 20 M/F: Centrilobular hypertrophy of hepatocytes
	One-year chronic toxicity study	0, 4, 20, 100	M/F: 4 M/F: Suppressed body weight	M/F: 4 M/F: Suppressed body weight
ADI			NOAEL: 4 SF: 100 ADI: 0.04	NOAEL: 4 SF: 100 ADI: 0.04
The critical study for setting ADI			One-year chronic toxicity study in dogs	One-year chronic toxicity study in dogs

ADI, Acceptable daily intake; NOAEL, No-observed-adverse-effect level; SF, Safety factor

[1)] The adverse effect observed at LOAEL

Table 2. *Potential adverse effects of a single oral administration of tiadinil*

Species	Study	Dose (mg/kg bw or mg/kg bw/day)	Endpoints relevant to setting NOAEL and ARfD (mg/kg bw or mg/kg bw/day) [1]
Rat	Acute toxicity study	M/F: 1 600, 2 240, 3 140, 4 390, 6 150	- M/F: Reduced locomotive activity, proneness
	Developmental toxicity study	F: 0, 30, 150, 750	Dams: 150 Dams: Decreased/suppressed body weight, decreased feed intake
Rabbit	Developmental toxicity study	F: 0, 30, 150, 600	Dams: 150 Dams: Decreased/suppressed body weight
ARfD			NOAEL: 150 SF: 100 ARfD: 1.5
The critical study for setting ARfD			(1) Developmental toxicity study in rats (2) Developmental toxicity study in rabbits

ARfD, Acute reference dose; NOAEL, No-observed-adverse-effect level; SF, Safety factor;
-, NOAEL could not be specified

1) The adverse effect observed at LOAEL