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

Risk Assessment Report

Florasulam

(Pesticides)

Food Safety Commission of Japan (FSCJ)
January 2022

ABSTRACT

The FSCJ conducted the risk assessment of florasulam (CAS No. 145701-23-1), an herbicide with a triazolopyrimidine ring, based on various documents.

The test used in the assessment includes the data on fate in animals (rats, goats and chicken), fate in plants (wheat), residues in crops, acute neurotoxicity (rats), subacute toxicity (rats, mice and dogs), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity/neurotoxicity (rats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), genotoxicity, immunotoxicity (rats), and others.

Based on the results of various toxicity studies, major adverse effects of florasulam observed were body weight (suppression of gain); kidneys (weight gain, hypertrophy of collecting duct cells); and adrenal glands (vacuolation of the zona resticularis and zona fasciculate in dogs). No neurotoxicity, carcinogenicity, reproductive toxicity, teratogenicity, genotoxicity and immunotoxicity were observed.

From the above results, florasulam (parent compound only) was identified as the relevant substance for the residue definition for dietary risk assessment in agricultural and livestock products.

The lowest value of the no-observed-adverse-effect level (NOAEL) in all toxicity studies was 4.9 mg/kg bw per day in one-year chronic toxicity study in dogs. On the basis of this value, the FSCJ specified an acceptable daily intake (ADI) of 0.049 mg/kg bw per day by applying a safety factor of 100.

For the possible adverse effects caused by the single oral administration, the NOAEL was 1,000 mg/kg bw in acute neurotoxicity study in rats, above the cut off value of 500 mg/kg bw. Accordingly, the FSCJ concluded that it was unnecessary to specify an acute reference dose (ARfD).

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

Species	Study	Dose (mg/kg bw per day)	NOAEL (mg/kg bw per day)	LOAEL (mg/kg bw per day)	Critical endpoints[1)]
Rat	90-day subacute toxicity study	M: 0, 20, 100, 500, 1 000 F: 0, 20, 100, 500, 800 M: 0, 19.4, 100, 485, 1 000 F: 0, 19.2, 98.0, 475, 1 030	M: 100 F: 98.0	M: 485 F: 475	M/F: Suppressed body weight, hypertrophy of the renal collecting duct cells
	Two-year combined chronic toxicity /carcinogenicity study	M: 0, 10, 250, 500 F: 0, 10, 125, 250 M: 0, 10.2, 254, 506 F: 0, 10.2, 127, 254	M/F: 10.2	M: 254 F: 127	M/F: Hypertrophy of the renal collecting duct cells (No carcinogenicity, no chronic neurotoxicity)
	Two-generation reproductive toxicity study	0, 10, 100, 500	Parent: 100 Offspring:500	Parent: 500 Offspring: -	Parent: Hypertrophy of the renal collecting duct cells, renal papilla inflammation and necrosis, etc. Offspring: No toxicity (No effect on reproductive ability)
	Developmental toxicity study	0, 50, 250, 750	Dams: 250 Fetuses: 750	Dams: 750 Fetuses: -	Dams: Suppressed body weight, decreased feed intake, increases in absolute and relative weights of the kidneys, etc. Fetuses: No toxicity (No teratogenicity)

Species	Study	Dose (mg/kg bw per day)	NOAEL (mg/kg bw per day)	LOAEL (mg/kg bw per day)	Critical endpoints[1)]
Mouse	90-day subacute toxicity study	0, 20, 100, 500, 1 000 M: 0, 22, 110, 549, 1 130, F: 0, 20, 101, 503, 1 010	M: 110 F: 503	M: 549 F: 1010	M/F: Hypertrophy of the renal collecting duct cells
	Two-year carcinogenicity study	0, 50, 500, 1 000 M: 0, 50.5, 505, 1 010 F: 0, 50.9, 497, 1 020	M: 50.5 F: 50.9	M: 505 F: 497	M/F: Hypertrophy of the renal collecting duct cells (No carcinogenicity)
Rabbit	Developmental toxicity study	0, 50, 250, 500	Dams: 500 Fetuses: 500	Dams:- Fetuses:-	Dams and Fetuses: No toxicity (No teratogenicity)
Dog	90-day subacute toxicity study	0, 5, 50,100 M: 0, 6, 56, 104 F: 0, 5, 55, 94	M: 6 F: 5	M: 56 F: 55	Hypertrophy of epithelial cells in the inner part of the outer layer of the renal medulla, etc.
	One-year chronic toxicity study	0, 0.5, 5, 100/50 0, 0.5, 4.9, 71.4	M/F: 4.9	M/F: 71.4	M/F: Decreased body weight, decreased feed intake,hypertrophy of the renal collecting duct cells, adrenal gland vacuolation of the zona reticularis and zona fasciculate
ADI			NOAEL: 4.9 SF: 100 ADI: 0.049		
The critical study for setting ADI			One-year chronic toxicity study (dog)		

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

[1)] The adverse effect observed at LOAEL

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

Species	Study	Dose (mg/kg bw)	Endpoints relevant to setting NOAEL and ARfD (mg/kg bw)[1)]
Rat	Acute toxicity study	1 000, 3 000, 6 000	M/F: 3 000 M/F: Death
	Acute neurotoxicity study	0, 200, 1 000, 2 000	M: 1 000 M: Decreased activity, decreased sensory (audition) function (FOB) and decreased motor activity
Mouse	Acute toxicity study	M: 5 000 F: 600, 2 000, 5 000	F: 2 000 F: Death
ARfD			Not required (Above cut off level (500 mg/kg bw))

FOB: Functional observation battery
ARfD: Acute reference dose
[1)] The adverse effect observed at LOAEL