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

Risk Assessment Report

Inpyrfluxam
(Pesticides)

Food Safety Commission of Japan (FSCJ)
October 2018

ABSTRACT

FSCJ conducted the risk assessment of a fungicide, inpyrfluxam (CAS No. 1352994-67-2), based on various documents.

The data used in the assessment include fate in animals (rats, goats and chicken), fate in plants (paddy rice and soy beans), residues in crops, subacute toxicity (rats, mice and dogs), acute and subacute neurotoxicity (rats), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), genotoxicity, effects on liver metabolism enzyme inductions and on steroid hormones and their receptors, and phototoxicityy.

Major adverse effects of inpyrfluxam observed are suppressed body weight and diffuse hepatocellular hypertrophy. Carcinogenicity, reproductive effects, teratogenicity and genotoxicity were not observed. Based on the results of various studies, inpyrfluxam (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.

The lowest no-observed-adverse-effect level (NOAEL) obtained in all toxicity studiess was 6 mg/kg bw/day in a one-year chronic toxicity study in dogs. FSCJ specified an ADI of 0.06 mg/kg bw/day for inpyrfluxam by applying a safety factor of 100 to the NOAEL.

The lowest level among NOAEL and lowest-observed-adverse-effect level (LOAEL) for potential adverse effects of a single oral administration of inpyrfluxam was the NOAEL of 30 mg/kg bw obtained in acute neurotoxicity studies in rats. FSCJ specified an acute reference dose (ARfD) to be 0.3 mg/kg bw by applying a safety factor of 100 to the NOAEL.

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

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
Rats	90-day subacute toxicity study	0, 150, 500, 2 000, 4 000 ppm M : 0, 9.72, 31.7, 123, 255 F : 0, 11.5, 37.5, 144, 296	M : 31.7 F : 37.5	M : 123 F : 144	M/F : Diffused hepatocellular hypertrophy
	90-day subacute neurotoxicity study	0, 500, 1 000 (F), 2 000, 4 000 (M) ppm M : 0, 30.0, 119, 240 F : 0, 35.2, 68.0, 133	M : 119 F : 35.2	M : 240 F : 68.0	M/F : Suppressed body weight, and decreased feed consumption
	Combined two-year chronic toxicity/carcinogenicity study	0, 150, 500, 1 500/1 000 (F), 2 000 (M) ppm M : 5.85, 19.4, 78.4 F : 7.47, 25.5, 65.8	M : 19.4 F : 25.5	M : 78.4 F : 65.8	M/F : Suppressed body weight (No carcinogenicity was observed)
	Two-generation reproductive toxicity study	0, 150, 500, 2 000 (M)/ 1 250 (F) ppm PM : 0, 9.38, 31.3, 124 PF : 0, 10.9, 35.5, 86 F_1M : 0, 11.6, 38.7, 156 F_1F : 0, 12.2, 41.4, 103	Parent and offspring PM : 31.3 PF : 35.5 F_1M : 38.7 F_1F : 41.4	Parent and offspring PM : 124 PF : 86 F_1M : 156 F_1F : 103	Parent and offspring: Suppressed body weight (No effect on reproductivity)
	Developmental toxicity study (the 1st study)	0, 10, 25, 80	Dams/Fetuses : 25	Dams/Fetuses : 80	Dams : Suppressed body weight and decreased feed consumption Fetuses : Low body weight (No teratogenicity)
	Developmental toxicity study (the 2nd study)	0, 90	Dams/Fetuses: -	Dams/Fetuse : 90	Dams : Staggering gait, weight loss, suppressed body weight, and decreased feed consumption Fetuses : Low body weight
Mice	90-day subacute toxicity study	0,200, 800, 3 500, 7 000 ppm M : 0, 27.2, 111, 491, 973 F : 0, 31.7, 130, 559, 1 100	M : 111 F : 130	M : 491 F : 559	M : Centrilobular hypertrophy of hepatocytes and fatty degeneration in the liver F : Decreased Alb

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
	18-month carcinogenicity study	0, 700, 2 000, 7 000/ 5 000 ppm M : 0, 77.0, 224, 775 F : 0, 69.3, 210, 701	M : 224 F : 69.3	M : 775 F : 210	M : Systemic amyloidosis F : Amyloidosis of the cervical lymph node and glandular stomach (No carcinogenicity)
Rabbits	Developmental toxicity study	0, 20, 60, 200	Dams : 60 Fetuses : 200	Dams : 200 Fetuses : -	Dams : abortion, weight loss/suppressed body weight, decreased feed consumption Fetuses : No toxicity (No teratogenicity)
Dogs	90-day subacute toxicity study	0, 40, 160, 700/500	M/F : 40	M/F : 160	M/F : Diffused hepatocellular hypertrophy in the liver
	One-year chronic toxicity study	0, 2, 6, 30, 160	M/F : 6	M/F : 30	M/F : Vacuolization of the adrenal fasciculata cells
ADI			NOAEL : 6 SF : 100 ADI : 0.06		
The critical study for setting ADI			One year chronic toxicity study in dogs		

ADI, Acceptable daily intake; SF, Safety factor; NOAEL, No-observed-adverse-effect level[1)],
The adverse effect observed at LOAEL