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

Risk Assessment Report

Esprocarb (Fourth edition)

(Pesticides)

Food Safety Commission of Japan (FSCJ)

June 2024

ABSTRACT

The FSCJ conducted a risk assessment of esprocarb (CAS No. 85785-20-2), a thiocarbamate herbicide, based on results from submitted documents. For this fourth edition, a request for reevaluation was made in accordance with the Agricultural Chemicals Regulation Act, whereby additional test results were submitted by the Ministry of Agriculture, Forestry and Fisheries including residues in soil, residues in crops (wheat and forage rice), fate in livestock (goats and chickens), acute toxicity (oral administration in rats) and reverse mutation, as well as reports on published scientific literature.

Test results used in the assessment include fate in plants (paddy rice, Japanese millet and wheat), residues in crops, fate in livestock (goats and chickens), fate in animals (rats), acute toxicity (rats and mice), subacute toxicity (dogs and rats), subacute neurotoxicity (rat), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mouse), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), and genotoxicity.

Major adverse effects of esprocarb were observed in the liver (increased organ weight, etc.,) and the kidneys (hyaline droplet depositions, etc.). Neither neurotoxicity, carcinogenicity, effects on fertility, nor genotoxicity was observed.

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

The lowest no-observed-adverse-effect level (NOAEL) obtained from these studies was 1 mg/kg bw per day in a one-year chronic toxicity study in dogs. The FSCJ specified an acceptable daily intake (ADI) of 0.01 mg/kg bw per day by applying a safety factor of 100 to this NOAEL.

The lowest NOAEL for potential adverse effects of a single oral administration of esprocarb was 5mg/kg bw per day from a developmental toxicity study in rats. The FSCJ specified an acute reference dose (ARfD) of 0.05 mg/kg bw by applying a safety factor of 100 to this NOAEL.

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

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	0, 100, 600, 1 800, 5 400 ppm M: 0, 6, 37, 105, 328 F: 7, 41, 117, 356	M: - F: 7	M: 6 F: 41	M: Tubular epithelial hyperplasia (regenerative) and hyaline droplet deposition F: Increased specific liver weights, etc.
	Two-year combined chronic toxicity/ carcinogenicity study	0, 25, 125, 600, 1 800 ppm M: 0, 1.1, 4.9, 24, 73 F: 0, 1.1, 5.5, 28, 85	M: 1.1 F: 5.5	M: 4.9 F: 28	M/F: Suppressed body weight gain and decreased food consumption (No carcinogenicity observed)
	90-day subacute neurotoxicity study	0, 200, 1 000, 5 000 ppm M: 0, 14, 70, 352 F: 0, 15, 72, 367	M: 352 F: 367	M: - F: -	No toxicity (No neurotoxicity observed)
	Two-generation reproductive toxicity study	0, 5, 25, 125, 600 ppm PM: 0, 0.29, 1.45, 7.2, 34 PF: 0, 0.33, 1.69, 8.4, 38 F1M: 0, 0.29, 1.43, 7.2, 35 F1F: 0, 0.34, 1.73, 8.7, 41	Parent PM: 1.45 PF: 8.4 F_1M: 1.43 F_1F: 8.7 Offspring PM: 7.2 PF: 8.4 F_1M: 7.2 F_1F: 8.7	Parent PM: 7.2 PF: 38 F_1M: 7.2 F_1F: 41 Offspring PM: 34 PF: 38 F_1M: 35 F_1F: 41	Parent M: Histopathological changes in the kidney, etc. F: Suppressed body weight gain, etc. Offspring M/F: Low body weight (No effect on fertility observed)
	Developmental toxicity study	0, 5, 50, 500	Dams: 5 Fetuses: 50	Dams: 50 Fetuses: 500	Dams: Suppressed body weight gain and decreased food consumption Fetuses: Low body weight (No teratogenicity observed)
Mouse	18-month carcinogenicity study	0, 25, 250, 2 400 ppm M: 0, 2.8, 27, 274 F: 0, 3.4, 34, 342	M: 2.8 F: 34	M: 27 F: 342	M: Colored rhinorrhea F: Increased renal papillary calcification, etc. (No carcinogenicity observed)
Rabbit	Developmental toxicity study	0, 20, 100, 200	Dams: 100 Fetuses: 100	Dams: 200 Fetuses: 200	Dams: Abortion, suppressed body weight gain, etc. Fetuses: Increase in late-stage resorption, etc. (No teratogenicity observed)
Dog	90-day subacute toxicity study	0, 10, 45, 200, 500	M: 10 F: 10	M: 45 F: 45	M/F: Eosinophilic changes/hypertrophy of hepatocytes, etc.

	One-year chronic toxicity study	0, 1, 8, 64	M: 1 F: 8	M: 8 F: 64	M: Hyperplasia and hypertrophy of the adrenal cortex F: Absolute and specific weight increases of the liver, etc.
ADI			NOAEL: 1 SF: 100 ADI: 0.01		
The critical study for setting ADI			One-year chronic toxicity study (dog)		

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

[1)] The adverse effect observed at LOAEL

-: NOAEL or LOAEL could not be specified.

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

Species	Study	Dose (mg/kg bw or mg/kg bw per day)	Endpoints relevant to setting NOAEL and ARfD (mg/kg bw or mg/kg bw per day)[1)]
Rat	Acute toxicity study	M: 2 276, 2 959, 3 846, 5 000, 6 500, 8 450, 10 985 F: 1 347, 1 751, 2 276, 2 959, 3 846, 5 000, 6 500	M: - F: - M/F: Decreased momentum in locomotor activities, blepharophimosis, lacrimation, etc.
	Acute toxicity study	F: 2 000	F: - Suppressed body weight gain
	Developmental toxicity study	F: 0, 5, 50, 500	Dams: 5 Dams: Decreased body weight and food intake
Mouse	Acute toxicity study	M: 3 641, 4 734, 6 154, 8 000, 10 400, 13 520, 17 576 F: 4 734, 6 154, 8 000, 10 400, 13 520	M/F: - M/F: Crouching position, decreased momentum) in locomotor activity, unkempt fur, etc.
	General pharmacology study (locomotor activity)	0, 250, 500, 1 000, 2 000, 4 000, 8 000	M/F: - M/F: Decreased grip strength
Rabbit	Developmental toxicity study	0, 20, 100, 200	Dams: 100 Dams: Decreased weight and food intake
Dog	90-day subacute toxicity study	0, 10, 45, 200, 500	M/F: 200 M/F: Decreased body weight
ARfD			NOAEL: 5 SF: 100 ARfD: 0.05
The critical study for setting ARfD			Developmental toxicity study (rat)

ARfD, Acute reference dose; NOAEL, No-observed-adverse-effect level; SF, Safety factor
[1)] The adverse effect observed at LOAEL
-: NOAEL could not be specified.