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

Risk Assessment Report

Thiobencarb (Third edition)

(Pesticides)

Food Safety Commission of Japan (FSCJ)
November 2023

ABSTRACT

The FSCJ conducted a risk assessment of thiobencarb (CAS No. 28249-77-6), a thiocarbamate herbicide, based on submitted documents. For this third 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 fate in livestock (goats and chickens) and reports on published scientific literature.

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

Major adverse effects of thiobencarb were observed in the liver (including organ weight gain and hepatocellular hypertrophy in rats and mice), and the kidneys (including hyaline droplet deposits in rats). Neither carcinogenicity, effects on fertility, teratogenicity nor biologically significant genotoxicity was observed.

Although abnormal gait and reduced sensory response were observed in the acute neurotoxicity study in rats, no neurotoxic effects were observed in the 90-day subacute neurotoxicity study.

Based on these results, thiobencarb (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 0.9 mg/kg bw per day in a two-year combined chronic toxicity/carcinogenicity study in rats. The FSCJ specified an acceptable daily intake (ADI) of 0.009 mg/kg bw per day by applying a safety factor of 100 to this NOAEL.

NOAEL and lowest-observed-adverse-effect level (LOAEL) values across these studies were compared for potential adverse effects of a single oral administration of thiobencarb, of which the lowest value was a

NOAEL of 100 mg/kg bw in an acute neurotoxicity study in rats. The FSCJ specified an acute reference dose (ARfD) of 1 mg/kg bw by applying a safety factor of 100 to this NOAEL.

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

Species	Study	Dose (mg/kg bw per day)	NOAEL (mg/kg bw per day)[1)]	Reference (Dossier for pesticides evaluation)
Rat	90-day subacute toxicity study	0, 250, 750, 2 250 ppm M: 0, 15.0, 44.2, 131 F: 0, 17.5, 51.8, 160	M: - F: - M/F: Suppressed body weight gain, etc.	M: - F: - M/F: Suppressed body weight gain, etc.
	Six-month subacute toxicity study	0, 30, 100, 300, 1 000 ppm M: 0, 2.5, 8.5, 25.4, 83.8 F: 0, 2.8, 8.6, 26.7, 90.2	M: 2.5 F: 2.8 M/F: Suppressed body weight gain, etc.	M: 2.5 F: 2.8 M/F: Suppressed body weight gain, etc.
	Two-year combined chronic toxicity/carcinogenicity study	0, 20, 100, 500 ppm M: 0, 0.9, 4.3, 22 F: 0, 1.0, 5.4, 26	M: 0.9 F: 1.0 M/F: Suppressed body weight gain, etc. (No carcinogenicity is observed.)	M: 0.9 F: 1.0 M/F: Suppressed body weight gain, etc. (No carcinogenicity is observed.)
	90-day subacute neurotoxicity study	0, 2, 20, 100	M/F: 2 M: Increased absolute and relative weights of the liver, etc. F: Suppressed body weight gain, etc. (No neurotoxicity is observed.)	M/F: 2 M: Increased absolute and relative weights of the liver, etc. F: Suppressed body weight gain, etc. (No neurotoxicity is observed.)
	Two-generation reproductive toxicity study	0, 2, 20, 100	Parents M/F: 2 Offspring M/F: 20 Parents M/F: Increased absolute and relative weights of the liver, etc. Offspring M/F: Delayed eye opening, etc. (No effect on fertility is observed.)	Parents M/F: 2 Offspring M/F: 100 Parents M/F: Increased absolute and relative weights of the liver, etc. Offspring M/F: No toxicity (No effect on fertility is observed.)
	Developmental toxicity study	0, 5, 25, 150	Dams and Fetuses: 25 Dams: Suppressed body weight gain Fetuses: Low body weight and increased sternal segment variation (No teratogenicity observed.)	Dams and Fetuses: 25 Dams: Suppressed body weight gain Fetuses: Low body weight and increased sternal variation (No teratogenicity observed.)

Mouse	90-day subacute toxicity study	0, 30, 100, 300, 3 000 ppm M: 0, 6.7, 16.7, 50.0, 517 F: 0, 4.0, 16.0, 48.0, 500	M: 16.7 F: 48.0 M: Increased absolute and relative weights of the testes F: Suppressed body weight gain, etc.	
	Two-year carcinogenicity study	0, 25, 100, 400, 1 600 ppm M: 0, 2, 10, 40, 166 F: 0, 3, 11, 42, 191	M: 2 F: 3 M/F: Histopathological changes in the liver (No carcinogenicity is observed.)	M: 40 F: 42 M/F: Suppressed body weight gain, decreased food intake (No carcinogenicity is observed.)
Rabbit	Developmental toxicity study	0, 20, 100, 200	Dams: 100 Fetuses:200 Dams: Increased absolute and relative weights of the liver Fetuses: No toxicity (No teratogenicity observed.)	Dams: 100 Fetuses:200 Dams: Increased absolute and relative weights of the liver Fetuses: No toxicity (No teratogenicity observed.)
Dog	28-day subacute toxicity study	0, 1, 4, 16, 64	M: 16 F: 1 M: Suppressed body weight gain, etc. F: Salivation	M: 16 F: 1 M: Suppressed body weight gain, etc. F: Salivation
	One-year chronic toxicity study	0, 1, 8, 64	M/F: 1 M: Decreases in TP and Alb F: Suppressed body weight gain	M/F: 1 M: Decreases in TP F: Suppressed body weight gain
ADI (cRfD)			NOAEL: 0.9 ADI: 0.009 SF: 100	NOAEL: 0.9 ADI: 0.009 SF: 100
The critical study for setting ADI (cRfD)			Two-year combined chronic toxicity/carcinogenicity study (rat)	Two-year combined chronic toxicity/carcinogenicity study (rat)

ADI, Acceptable daily intake; Alb, albumin; cRfD, Chronic reference dose; NOAEL, No-observed-adverse-effect level; SF, Safety factor; TP, total protein
[1)] The adverse effect observed at LOAEL.
-, NOAEL could not be specified.

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

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	539, 700, 910, 1 183, 1 538	M/F: - Red erosions on eyelids, piloerection, loss of luster in fur, prone and lateral positions
	Acute toxicity study	579, 694, 833, 1 000, 1 200, 1 440, 1 728	M/F: - M/F: Sedation, abnormal gait, dyspnea, ptosis, etc.
	Acute neurotoxicity study	0, 100, 500, 1 000	M/F: 100 M/F: Abnormal gait, decreased locomotor activity, decrease in sensory response, etc.
Mouse	Acute toxicity study	910, 1 183, 1 538	M/F: - Piloerection, loss of luster in fur, prone and lateral positions
	General pharmacological study (general condition)	M: 0, 150, 300, 600	M: 150 Decreased locomotor activity and reduced hanging strength, decreased body temperature, stertor, passivity
	General pharmacological study (locomotor activity)	M: 0, 150, 300, 600	M: 150 Low locomotor activity
	90-day subacute toxicity study	0, 30, 100, 300, 3 000 ppm M: 0, 6.7, 16.7, 50.0, 517 F: 0, 4.0, 16.0, 48.0, 500	M: 50.0 F: 48.0 M/F: Piloerection and bradykinesia
	Comprehensive evaluation encompassing general pharmacological study (general condition), general pharmacological study (locomotor activity), and 90-day subacute toxicity study		150
ARfD			NOAEL: 100 SF: 100 ARfD: 1
The critical study for setting ARfD			Acute neurotoxicity 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.