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

Risk Assessment Report

Dichlobentiazox

(Pesticides)

Food Safety Commission of Japan (FSCJ)
May 2019

ABSTRACT

FSCJ established health based guidance values of dichlobentiazox (CAS No.957144-77-3), a fungicide which contains benzothiazole/isothiazole ring based on results from various studies in the risk assessment.

The data used in the assessment include fate in animals (rats), livestock (goats), fate in plants (paddy rice), residues in crops, subacute toxicity (rats, mice and dogs), chronic toxicity (dogs), chronic toxicity/carcinogenicity (fats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), and genotoxicity.

Major adverse effects of dichlobentiazox were suppressed body weight, anemia in dogs, hyperplasia and hypertrophy of bile duct in the liver, and epithelial hypertrophy/hyperplasia of villus in the duodenum. No carcinogenicity, reproductive toxicity, teratogenicity or genotoxicity was observed.

On the basis of various studies, dichlobentiazox (parent compound only) was identified as a relevant substance for residue definition for dietary risk assessment in agricultural product.

The lowest no-observed-adverse-effect level (NOAEL) obtained in all studies was 5.03 mg/kg bw/day in a two-year chronic toxicity/carcinogenicity study in rats. FSCJ specified an acceptable daily intake (ADI) of 0.05 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.

FSCJ judged it unnecessary to specify an acute reference dose (ARfD), since no adverse effects would be likely to be elicited by a single oral administration of dichlobentiazox.

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

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
Rat	90-day subacute toxicity study	0, 300, 900, 3 000 ppm M: 0, 22, 65, 236 F: 0, 25, 74, 263	M: 22 F: 74	M: 65 F: 263	M: Hyaline droplet accumulation in renal tubule cortex and others F: Epithelial villus hypertrophy/hyperplasia of duodenum
	Two-year combined chronic toxicity /carcinogenicity study	0, 120, 550, 2 500 ppm M: 0, 5.03, 23.5, 108 F: 0, 7.01, 31.9, 144	M: 5.03 F: 7.01	M: 23.5 F: 31.9	FM: Epithelial villus hypertrophy/hyperplasia of duodenum and others (Not carcinogenic)
	Two-generation reproductive toxicity study	0, 62.5, 250, 1 000	Parent M: 62.5 F: 1 000 Offspring FM: 1,000	Parent M: 250 F: — Offspring FM: —	Parent M: Suppressed body weight F: No toxicity Offspring FM: No toxicity (No effect on reproduction)
	Developmental toxicity	0, 62.5, 250, 1 000	Maternal: 250 Embryo/fetus: 250	Maternal: 1 000 Embryo/fetus: 1 000	Maternal: Suppressed body weight and decreased feed consumption Embryo/fetus: Delayed ossification (absent ossification of fifth and sixth sternebrae) (Not teratogenic)
Mouse	90-day subacute toxicity study	0, 100, 450, 2 000 ppm M: 0, 14, 65, 315 F: 0, 19, 80, 381	M: 65 F: 80	M: 315 F: 381	FM: Epithelial villus hypertrophy/hyperplasia of duodenum and others
	78-week carcinogenicity study	0, 50, 325, 2 000 ppm M: 0, 5.8, 38, 247 F: 0, 6.6, 42, 258	M: 247 F: 258	M: — F: —	FM: No toxicity (Not carcinogenic)
Rabbit	Developmental toxicity study	0, 15, 50, 150	Maternal: 50 Embryo/fetus: 150	Maternal: 150 Embryo/fetus: —	Maternal: Decreased/suppressed body weight, decreased feed consumption and others Embryo/fetus: Not toxic (Not teratogenic)
Dog	90-day subacute toxicity study	0, 10, 70, 500	FM: 10	FM: 70	FM: Bile duct hyperplasia in liver

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
	One-year chronic toxicity study	0, 5, 50, 500/200	FM: 50	FM: 500/200	M: Bile duct hypertrophy in liver and others F: Decreased RBC, Ht or Hb and others
ADI			NOAEL: 5.03 SF: 100 ADI: 0.05		
The critical study for setting the ADI			Two-year combined chronic toxicity/carcinogenicity study in rats		

ADI, Acceptable daily Intake; NOAEL, No-observed-adverse-effect level; SF, Safety Factor;
－, Lowest-observed-adverse-effect level (LOAEL) was not derived;
[1)], The adverse effect observed at LOAEL