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

Risk Assessment Report

MCPB

(Pesticides)

Food Safety Commission of Japan (FSCJ)
September 2018

ABSTRACT

FSCJ established health based guidance values of MCPB-ethyl (CAS No.10443-70-6), a phenoxy herbicide based on results from various studies in the risk assessment of MCPB.

The data used in the assessment include fate in animals (rats), fate in plants (paddy rice, apples and others), residue in crops, subacute toxicity (rats, mice and dogs), subacute neurotoxicity (rats), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits) and genotoxcity.

Major adverse effects of MCPB-ethyl are suppressed body weight and increased kidney weights.
No neurotoxicity, carcinogenicity, reproductive toxicity and genotoxicity was observed.

MCPB-ethyl, at the dose with maternal toxicity, caused increase in ventricular septal defects in a developmental toxicity study in rats. No teratogenicity was observed in a developmental toxicity study in rabbits.

On the basis of various studies, MCPB-ethyl, its metabolite B and C were identified as relevant substances for residue definition for dietary risk assessment in agricultural products.

The lowest no-observed adverse effect level (NOAEL) obtained in all studies was 1.24 mg/kg bw/day in the first two-generation reproductive toxicity study in rats. FSCJ specified an acceptable daily intake (ADI) of 0.012 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.

The lowest NOAEL for adverse effects of eliciting a single oral administration of MCPB-ethyl was 20 mg/kg bw/day obtained in a maternal effect in the developmental toxicity study in rabbits. FSCJ specified an acute reference dose (ARfD) to be 0.2 mg/kg bw by applying a safety factor of 100 to the NOAEL.

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

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day) Critical endpoints[1)]
Rat	13-week subacute toxicity study	0, 5, 25, 100, 400	FM : 100 FM : Suppressed body weight and periportal cell infiltration in the liver
	28-day subacute neurotoxicity study	0, 200, 800, 4 000 ppm M : 0, 18, 71, 347 F : 0, 19, 74, 336	General toxicity M : 71 F : 74 FM : Suppressed body weight, decreased feed consumption and others (Not neurotoxic)
	Two-year combined chronic toxicity/carcinogenicity study	0, 100, 400, 1 200 ppm M : 0, 4.69, 19.2, 57.9 F : 0, 6.02, 23.9, 76.1	M : 19.2 F : 23.9 FM : Suppressed body weight and others (Not carcinogenic)
	Two-generation reproductive toxicity study (the 1st study)	0, 15, 75, 375 ppm PM : 0, 0.94, 4.76, 23.6 PF : 0, 1.24, 6.14, 31.4 F_1M : 0, 1.10, 5.52, 27.2 F_1F : 0, 1.32, 6.59, 32.8	Parent PM : 4.76 PF : 1.24 F_1M : 5.52 F_1F : 1.32 Offspring PM : 23.6 PF : 31.4 F_1M : 27.2 F_1F : 32.8 Parent M : Decreased absolute/relative adrenal weight F : Suppressed body weight Offspring No toxicological effects (No effect on reproduction)

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day) Critical endpoints[1)]
	Developmental toxicity study	0, 10, 50, 250	Maternal and Embryo/fetus : 50 Maternal : Suppressed body weight and others Embryo/fetus : Decreased body weight and others (Increased ventricular septal defect)
Mouse	13-week subacute toxicity study	0, 10, 50, 125, 500	FM : 500 FM : No toxicological effects
	78-week carcinogenicity study	0, 400, 1 200, 3 600 ppm --- M : 0, 53.4, 175, 512 F : 0, 78.6, 226, 592	M : 53.4 F : － M : Increased absolute/relative kidney weight F : Suppressed body weight and others (Not carcinogenic)
Rabbit	Developmental toxicity study	0, 5, 20, 80	Maternal : 20 Embryo/fetus : 80 Maternal : Low body weight/Suppressed body weight and others Embryo/fetus : No toxicological effects (Not teratogenic)
Dog	90-day subacute toxicity study	0, 100, 300, 2 000 ppm --- M : 0, 2.45, 7.47, 51.9 F : 0, 2.70, 8.51, 55.0	M : 7.47 F : 2.70 M : Decreased absolute/relative testis, epididymides and prostate weights and others F : Decreased body weight and others
ADI			NOAEL : 1.24 SF : 100 ADI : 0.012
The critical study for setting the ADI			Two-generation reproductive toxicity study in rats (the 1st study)

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

Table 2. *Adverse effect possibly elicited by a single oral administration*

Species	Study	Dose (mg/kg bw or mg/kg bw/day)	NOAEL and end point for establishing acute reference dose (ARfD)[1)] (mg/kg bw or mg/kg bw/day)
Rat	General pharmacology data (Central nervous system)	0, 125, 500, 2 000	M : 125 M : Hypothermia and gait abnormalities
Mouse	General pharmacology data (Motor coordination)	0, 125, 500, 2 000	M : 500 M : Decreased motor coordination
	General pharmacology data (Locomotion activity)	0, 31.3, 125, 500	M : 125 M : Decreased locomotion activity
Rabbit	Developmental toxicity study	0, 5, 20, 80	Maternal : 20 Maternal : Decreased body weight, crouching posture and others
ARfD			NOAEL : 20 SF : 100 ARfD : 0.2
The critical study for setting ARfD			Developmental toxicity study in rabbits

ARfD, Acute reference dose; SF, Safety factor; NOAEL, No-observed adverse effect level;

[1)],The adverse effect observed at LOAEL.