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

Risk Assessment Report

Chlormequat

(Pesticides)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted a risk assessment of chlormequat (CAS No. 999-81-5), a plant growth regulator, based on results from various studies.

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

Major adverse effects of chlormequat were suppressed body weight, effects on the nervous system including tremor and salivation. Chlormequat showed no carcinogenicity, teratogenicity or genotoxicity.

Decrease in conception rate and reduced mean numbers of pups per litter were observed in rats in a two-generation reproductive toxicity study.

Based on various studies, chlormequat (parent compound only) was identified as the relevant substance for the residue definition for dietary risk assessment in agricultural products.

The lowest no-observed-adverse-effect level (NOAEL) obtained in all studies was 5 mg/kg bw/day in a one-year chronic toxicity study in dogs and a first developmental toxicity study in rabbits. FSCJ specified an acceptable daily intake (ADI) of 0.05 mg/kg bw/day, applying a safety factor of 100 to the NOAEL.

The lowest NOAEL for adverse effects elicited by a single oral administration of chlormequat was 5 mg/kg bw/day in the one-year chronic toxicity study in dogs. Consequently, FSCJ specified an acute reference dose (ARfD) of 0.05 mg/kg bw, applying a safety factor of 100 to the NOAEL.

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

Species	Study	Dose (mg/kg bw/day)	NOAEL(mg/kg bw/day) and Critical endpoints[1)]
Rat	90-day subacute toxicity (the 1st study)	0, 300, 900, 2 700, 8 100, 24 300 ppm M : 0, 20.6, 61.3, 189, 586, 607 F : 0, 24.4, 72.9, 220, 623, 577	M: 61.3 F: 220 FM: Suppressed body weight and decreased feed consumption
	90-day subacute neurotoxicity study	0, 400, 1 200, 3 600/4 200 ppm M: 0, 27.4, 82.5, 261 F: 0, 31.1, 90.0, 299	M: 82.5 F: 90.0 FM: Suppressed body weight and others
	18-month chronic toxicity study	0, 281, 937, 2 811 ppm M: 0, 13, 43, 136 F: 0, 17, 56, 172	M: 43 F: 56 FM: Suppressed body weight
	Two-year carcinogenicity study	0, 281, 937, 2 811 ppm M: 0, 13, 42, 125 F: 0, 16, 55, 173	M: 42 F: 55 FM: Suppressed body weight and decreased feed consumption (Not carcinogenic)
	Two-generation reproductive toxicity study	0, 300, 900, 2 700 ppm PM: 0, 28.9, 86.4, 255 PF: 0, 30.8, 93.4, 279 F_1M: 0, 28.8, 87.3, 286 F_1F: 0, 31.7, 95.8, 314	Parent and offspring: PM: 86.4 PF: 93.4 F_1M: 87.3 F_1F: 95.8 Reproductive ability: PM: 86.4 PF: 93.4 F_1M: 87.3 F_1F: 95.8 Parent: FM: Suppressed body weight and decreased feed consumption Offspring: Suppressed body weight and delay in physical/behavioral development Reproductive ability: Decreased conception rate /number of births
	Developmental toxicity (the 1st study)	0, 30, 90, 180	Maternal: 30 Embryo/fetus: 180 Maternal: Salivation, suppressed body weight and others

			Embryo/fetus: No toxicological effects (Not teratogenic)
Mouse	90-day subacute toxicity study	0, 472, 1 408, 4 212 ppm M : 0, 120, 370, 1 070 F : 0, 150, 470, 1 400	M: 1 070 F: 1 400 FM: No toxicological effects
	110-week combined chronic toxicity/carcinogenicity study	0, 150, 600, 2 400 ppm M : 0, 21, 84, 336 F : 0, 23, 91, 390	M: 336 F: 91 M: No toxicological effects F: Atrophic changes in the ovaries (Not carcinogenic)
Rabbit	Developmental toxicity (the 1st study)	0, 5, 20, 35	Maternal: 5 Embryo/fetus: 35 Maternal: Death and suppressed body weight Embryo/fetus: No toxicological effects (Not teratogenic)
	Developmental toxicity (the 2nd study)	0, 1.5, 3, 6, 12	Maternal: 6 Embryo/fetus: 12 Maternal: Suppressed body weight Embryo/fetus: No toxicological effects (Not teratogenic)
Dog	One-year chronic toxicity study	0, 150, 300, 1 000 ppm FM : 0, 5, 10, 32	FM: 5 FM: Salivation and others
ADI			NOAEL: 5 SF: 100 ADI: 0.05
The critical study for setting the ADI			One-year chronic toxicity study in dogs and developmental toxicity study in rabbits (the 1st study)

ADI, Acceptable daily intake; cRfD, Chronic reference dose; UF, Uncertainty factor; SF, Safety factor; NOAEL, No-observed-adverse-effect level; LOAEL, Lowest-observed-adverse-effect level;
-, NOAEL could not be specified; [1)], The adverse effect observed at LOAEL

Table 2. *Adverse effects 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	Acute toxicity study	0, 300, 600, 1 200, 2 400	FM: － FM: Salivation, decreased activity and others
		0, 383, 464, 562, 681, 825, 1 000, 1 210, 1 470, 1 780	FM: 383 FM: Mild diarrhea, writhing and others
	Acute neurotoxicity study	0, 30, 100, 300	FM: 100 FM: Reduced motor activity, dyspnea and others
	Developmental toxicity study (the 1st study)	0, 30, 90, 180	Maternal: 90 Maternal: Suppressed body weight, reduced motor activity, tremor, ataxia and others
Dog	One-year chronic toxicity study	0, 5, 10, 32	FM: 5 M: Diarrhea and salivation F: Salivation
ARfD			NOAEL: 5 SF: 100 ARfD: 0.05
The critical study for setting ARfD			One-year chronic toxicity study in dogs

ARfD, Acute reference dose; SF, Safety factor; NOAEL, No-observed-adverse-effect level
1), The adverse effect observed at LOAEL
－, NOAEL was not derived