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

Risk Assessment Report

Cyanophos
(Pesticides)

Food Safety Commission of Japan (FSCJ)
October 2017

ABSTRACT

FSCJ conducted a risk assessment of cyanophos (CAS No.2636-26-2), an organophosphorus insecticide, based on results from various studies.

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

The major adverse effect of cyanophos was inhibition of cholinesterase (ChE) activities in brain and red blood cells. Cyanophos has no carcinogenicity, reproductive toxicity, teratogenicity and genotoxicity relevant to human health.

Based on various studies, cyanophos (parent compound only) was a substance relavant to the residue definition for dietary risk assessment in agricultural products.

The lowest no-observed-effect level (NOAEL) obtained in all studies was 0.101 mg/kg bw/day in a combined two-year chronic toxicity/carcinogenicity study in rats. FSCJ specified an acceptable daily intake (ADI) of 0.001 mg/kg bw/day, applying a safety factor of 100 to the NOAEL.

The lowest NOAEL for adverse effects that would be likely to be elicited by a single oral administration of cyanophos was 1 mg/kg bw/day obtained in a study of the inhibition of ChE activity in rats. FSCJ specified an acute reference dose (ARfD) of 0.01 mg/kg bw/day, applying a safety factor of 100 to the NOAEL.

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

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
Rat	30-day subacute toxicity study	0, 10, 20, 70, 250 ppm M: 0, 0.75, 1.8, 6.5, 18.8 F: 0, 0.77, 1.7, 6.2, 21.6	M: 0.75 F: 0.77	M: 1.8 F: 1.7	F/M: Inhibition of brain cholinesterase (ChE) activity (20% or over)
	90-day subacute toxicity study	0, 10, 40, 160 ppm M: 0, 0.75, 2.8, 10.3 F: 0, 0.75, 2.9, 11.6	M: 0.75 F: 0.75	M: 2.8 F: 2.9	F/M: Inhibition of brain and erythrocyte ChE activity (20% or over)
	24-week subacute toxicity study	0, 10, 20, 60, 180 ppm M: 0, 0.56, 1.4, 3.8, 11.7 F: 0, 0.77, 1.5, 4.3, 12.7	M: 1.4 F: 0.77	M: 3.8 F: 1.5	F/M: Inhibition of brain ChE activity (20% or over) and others
	90-day subacute neurotoxicity study	0, 3, 20, 100 ppm M: 0, 0.20, 1.35, 7.25 F: 0, 0.26, 1.70, 8.83	M: 0.20 F: 0.26	M: 1.35 F: 1.70	F/M: Inhibition of brain and erythrocyte ChE activity (20% or over) and others
	Two-year chronic toxicity/carcinogenicity study	0, 3, 10, 30, 180 ppm M: 0, 0.101, 0.338, 1.04, 7.15 F: 0, 0.115, 0.403, 1.22, 9.09	M: 0.101 F: 0.115	M: 0.338 F: 0.403	F/M: Inhibition of brain ChE activity (20% or over) and others (Not carcinogenic)
	Two-generation reproductive toxicity study	0, 1, 3, 10, 25 ppm PM: 0, 0.08, 0.21, 0.68, 1.76 PF: 0, 0.10, 0.22, 0.79, 1.99 F_1M: 0, 0.11, 0.27, 0.85, 2.17	Parent PM: 1.76 PF: 0.79 F_1M: 2.17 F_1F: 0.95 Offspring PM: 0.68 PF: 0.79 F_1M: 0.85 F_1F: 0.95	Parent PM: - PF: 1.99 F_1M: - F_1F: 2.53 Offspring PM: 1.76 PF: 1.99 F_1M: 2.17 F_1F: 2.53	Parent M: No toxicity F: Suppressed body weight and others Offspring: Decrease in survival rate, suppressed body weight and others (No effect on reproduction)

		F_1F: 0, 0.11, 0.28, 0.95, 2.53			
	Developmental toxicity study (the 1st study)	0, 1, 3, 10	Maternal: 3 Embryo/fetus: 10	Maternal: 10 Embryo/fetus: -	Maternal: Suppressed body weight and others Embryo/fetus: No toxicity (Not teratogenic)
Mouse	Two-year chronic toxicity/carcinogenicity study	0, 1, 10, 100 ppm M: 0, 0.1, 1.5, 13.8 F: 0, 0.2, 1.9, 15.3	M: 1.5 F: 1.9	M: 13.8 F: 15.3	F/M: Inhibition of brain and erythrocyte ChE activity (20% or over) and others (Not carcinogenic)
Rabbit	Developmental toxicity study	0, 0.8, 2.5, 7.5	Maternal: 2.5 Embryo/fetus: 7.5	Maternal: 7.5 Embryo/fetus: -	Maternal: Death, ataxia, salivation and others Embryo/fetus: No toxicity (Not teratogenic)
Dog	One-year chronic toxicity study	0, 0.1, 0.3, 3	M: 0.3 F: 0.3	M: 3 F: 3	F/M: Inhibition of brain and erythrocyte ChE activity (20% or over)
ADI			NOAEL: 0.101 SF: 100 ADI: 0.001		
The critical study for setting the ADI			Two-year chronic toxicity/carcinogenicity study in rats		

M, Male; F, Female; F/M, both sexes; PM, Male in P (Parent) generation; PF, Female in P generation; F_1M, Male in F_1 generation; F_1F, Female in F_1 generation; ADI, Acceptable daily intake; SF, Safety factor; NOAEL, No-observed-adverse-effect level; -, NOAEL could not be specified
[1)] The adverse effect observed at LOAEL

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

Species	Study	Dose (mg/kg bw or mg/kg bw/day)	NOAEL (mg/kg bw or mg/kg bw/day) and critical endpoints[1)]
Rat	Acute toxicity study (the 1st study)	M: 10, 25, 50, 100, 200, 400, 600, 800, 1 000, 1 200 F: 10, 25, 50, 100, 200, 400, 600, 800, 1 000, 2 000	F/M: 10 F/M: Fasciculation, tremor, ataxic gate, salivation, piloerection, nasal hemorrhage, exophthalmos, reddish tear, and dyspnea
	Acute toxicity study (the 2nd study)	0, 2.5, 25, 250, 600, 750, 950, 1 200	F/M: 2.5 F/M: Decrease in locomotion activity, twitch, limb paralysis, ataxic gate, dyspnea, irregular respiration, piloerection, exophthalmos, lacrimation, miosis, salivation and incontinence of urine
	Acute neurotoxicity study	0, 4, 20, 80	F/M: 4 FM: Decreased activity and others
	ChE inhibition activity test	F: 0, 1, 2, 4	F: 1 Inhibition of ChE activity in red blood cell (20% or over)
Mouse	Acute toxicity study (the 2nd study)	0, 296, 385, 500, 650, 845, 1 100, 1 430	F/M: - F/M: Decrease in locomotion activity
	Acute toxicity study (the 3rd study)	0, 25, 100, 500, 700, 1 000, 1 400, 2 000	F/M: 100 F/M: Decrease in locomotion activity, twitch, tremor, clonic convulsion, limb paralysis, ataxic gate, irregular respiration, lacrimation, miosis, salivation, excretion of oily substance, and in continence of urine
Rabbit	Developmental toxicity study	0, 0.8, 2.5, 7.5	Maternal: 2.5 Maternal: Ataxia, salivation, miosis, lacrimation, stridor, tachypnea and loose stool
ARfD			NOAEL: 1 SF: 100 ARfD: 0.01
The critical study for setting the ARfD			ChE inhibition study in rats

ARfD, Acute reference dose; SF, Safety factor; NOAEL, No-observed-adverse-effect level; -, NOAEL could not be specified

[1)], The adverse effect observed at LOAEL