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

Risk Assessment Report

Chloropicrin

(Pesticides)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted the risk assessment of chloropicrin (CAS No. 76-06-2), a soil fumigant used as a fungicide, an insecticide, and an herbicide, based on various documents.

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

Chloropicrin has a serious irritating effect on eyes and skin in rabbits and a corrosive effect on rabbit skin. Major adverse effects of chloropicrin observed in the various toxicity studies were mucosal hyperplasia/hyperkeratosis in forestomach in rats and anemia in rats and dogs. There was no treatment related effect on reproduction or teratogenicity, and no genotoxicicity to humans. In carcinogenicity studies, increased incidences of bronchiolo-alveolar adenoma, carcinomas in the lung and Harderian gland adenomas in mice of both sexes, and squamous cell papillomas and carcinomas of forestomach in female mice were observed. However, a genotoxic mechanism was unlikely to be involved in tumor induction, and it was possible to establish a threshold dose in the assessment.
From the above results, chloropicrin (parent compound only) was identified as the relevant substance for the residue definition for dietary risk assessment in agricultural products.

The lowest value of the NOAEL in all tests was 0.1 mg/kg bw/day in a one-year chronic toxicity study in dogs. FSCJ specified an ADI of 0.001 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.
The lowest NOAEL and LOAEL for potential adverse effects of a single oral administration of chloropicrin was NOAEL of 50 mg/kg bw/day obtained in acute neurotoxicity studies in rats. FSCJ specified an acute reference dose (ARfD) to be 0.5 mg/kg bw by applying a safety factor of 100 to the NOAEL.

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

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, 4, 10, 25	M：10 F：4	M：25 F：10	M/F：Epithelial hyperplasia of mucosa, and Hyperkeratosis in the forestomach
	Two-year combined chronic toxicity/carcinogenicity study	0, 0.075, 0.75, 7.5	M：7.5 F：0.75	M：－ F：7.5	M：No toxic effect F：Erosion / ulceration, chronic active inflammation, and diffuse epithelial hyperplasia in the forestomach (No carcinogenicity)
	Two-generation reproductive toxicity study	0, 0.2, 1.0, 5.0	Parent M/F：1.0 Offspring：5.0	Parent M/F：5.0 Offspring：－	Parent M/F：Epithelial hyperplasia of mucosa in the forestomach Offspring：No toxic effect (No effect on reproductivity)
	Developmental toxicity study	0, 1, 5, 30	Dams：5 Fetuses：30	Dams：30 Fetuses：－	Dams：Salivation, Suppressed body weight Fetuses：No toxic effect (No teratogenicity)
Mouse	90-day subacute toxicity study	0, 8, 20, 50	M：50 F：50	M：－ F：－	M/F：No toxic effect

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
	78-week carcinogenicity study	0, 0.6, 6, 60/50/30	M：6 F：6	M：60/50/30 F：60/50/30	M/F：Epithelial hyperplasia of mucosa, and Hyperkeratosis in the forestomach (M/F：Bronchiolo-alveolar adenoma, carcinomas in the lung and Harderian gland adenomas of F：Increased incidences of squamous papillomas and carcinomas in the forestomach
Rabbit	Developmental toxicity study	0, 1, 3, 10	Dams：10 Fetuses：10	Dams：－ Fetuses：－	Dams：No toxic effect Fetuses：No toxic effect (No teratogenicity)
Dog	One-year chronic toxicity study	0, 0.1, 1.0, 5.0	M/F：0.1	M/F：1.0	M/F：Vomiting
ADI			NOAEL：0.1 SF：100 ADI：0.001		
The critical study for setting ADI			One-year chronic toxicity study in dogs		

－, LOAEL could not be specified.
[1)], The adverse effect observed at LOAEL

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

Species	Study	Dose (mg/kg bw or mg/kg bw/day)	Endpoints relevant to setting NOAEL and ARfD (mg/kg bw or mg/kg bw/day) [1)]
Rat	Acute toxicity	74, 104, 146, 204, 286, 400	M/F: － M/F: Sedation, lacrimation
	Acute neurotoxicity	0, 50, 125, 313	M/F: 50 M: Decreased locomotor activity F: Locomotor activity
Mouse	Acute toxicity	74, 104, 146, 204, 286, 400	M/F: － M/F: Sedation, lacrimation
ARfD			NOAEL: 50 SF: 100 ARfD: 0.5
The critical study for setting ARfD			Acute neurotoxicity study in rats

ARfD, Acute reference dose; NOAEL, No-observed-adverse-effect level; SF, Safety factor;
－, NOAEL could not be specified
[1)], The adverse effect observed at LOAEL