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

Risk Assessment Report

Kasugamycin (2nd Edition)

(Pesticides)

Food Safety Commission of Japan (FSCJ)
October 2020

ABSTRACT

FSCJ conducted a risk assessment of an aminoglycoside antibiotic, kasugamycin (CAS No.19408-46-9), based on various documents. Data on residue in crops (broccoli and cherries) were newly available in this assessment.

The data used in the assessment are on: fate in animals (rats and goats), fate in plants (paddy rice, tomatoes and others), residues in crops, subacute toxicity (rats, mice, dogs), subacute neurotoxicity (rats), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), genotoxicity and others.

Major adverse effects of kasugamycin observed are: decreased body weight gain, ulcer and inflammation in the rectum and anus, damage to the lingua (disappearance of the papillary epithelial cells in dogs), brown pigmentation in proximal tubular epithelial cells in the kidney, and tubular atrophy in the testes. No neurotoxicity, carcinogenicity, teratogenicity or genotoxicity was observed.

In a two-generation reproductive toxicity study in rats, the incidence of testicular toxicity such as tubular atrophy increased in F1 parental animals, and decrease in conception rate and others were observed.

FSCJ specified the residue definition for this dietary risk assessment in agricultural products to be kasugamycin (parent compound only).

The lowest no-observed-adverse-effect level (NOAEL) in the toxicological studies was 9.43 mg/kg body weight/day in a two-generation reproductive toxicity study in rats. Applying the safety factor of 100 to the lowest NOAEL, FSCJ specified the acceptable daily intake (ADI) to be 0.094 mg/kg body weight/day. Since the absence of any toxicological effects that would be likely elicited by a single dose of kasugamycin was observed, FSCJ considered it unnecessary to specify the ARfD.

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

Species	Study	Dose (mg/kg bw/day)[2)]	NOAEL (mg/kg bw/day)[1)]
			FSCJ
Rat	90-day subacute toxicity study	0, 300, 1 000, 3 000, 6 000 ppm M: 0, 11.3, 37.5, 114, 229 F: 0, 13.1, 44.6, 130, 255	M: 11.3 F: 13.1 M: Decreased Ht, Hb, and RBC F: Foamy cell aggregation in the lung
	90-day subacute neurotoxicity study	0, 300, 3 000, 6 000 ppm M: 0, 21, 210, 439 F: 0, 23, 238, 486	M: 210 F: 238 M/F: Suppressed body weight (No subacute neurotoxicity)
	Combined two-year chronic toxicity/carcinogenicity study	0, 30, 300, 3 000 ppm M: 0, 1.15, 11.3, 116 F: 0, 1.37, 13.4, 140	M: 11.3 F: 13.4 M/F: Increased brown pigmentation in renal proximal tubular epithelium cells in the kidney (No carcinogenicity)
	Two-generation reproductive toxicity study	0, 200, 1 000, 6 000 ppm PM: 0, 10.2, 51.0, 314 PF: 0, 17.6, 88.2, 561 F_1M: 0, 9.43, 46.0, 293 F_1F: 0, 17.9, 87.6, 538	Parent: PM: 10.2 PF: 88.2 F_1M: 9.43 F_1F: 87.6 Offspring: PM: 314 PF: 561 F_1M: 293 F_1F: 538 Parent : M: Suppressed body weight F: Uncler in the rectum Offspring: M/F: No toxicity Reproductive activity PM: 51.0 PF: 88.2 F_1M: 46.0 F_1F: 87.6 (decrease in conception rate with 6 000 ppm)

	Developmental toxicity study	0, 40, 200, 1 000	Dams: 200 Fetuses: 1 000 Dams: Suppressed body weight Fetuses: No toxicity was observed. (No teratogenicity)
Mouse	90-day subacute toxicity study	0, 300, 1 000, 3 000, 10 000 ppm	M: 87.7 F: 111
		M: 0, 26.7, 87.7, 265, 1 010 F: 0, 37.6, 111, 367, 1 190	M/F: Ulcer and inflammation
	78-week carcinogenicity study	0, 50, 300, 1 500 ppm	M: 22.7 F: 140
		M: 0, 3.85, 22.7, 121 F: 0, 4.71, 27.6, 140	M: Increased absolute- and relative-weight of the spleen F: No toxicity was observed (No carcinogenicity)
Rabbit	Developmental toxicity study	0, 1, 3, 10	Dams and fetuses: 10, the highest dose tested (No teratogenicity)
Dog	90-day subacute toxicity study	0, 300, 3 000, 6 000/4 500 ppm	M: 9.29 F: 10.0
		M: 0, 9.29, 92.9, 138, 186 F: 0, 10.0, 94.6, 152, 163	M/F: Disappearance of the papillary epithelial cells of the lingua
	One-year chronic toxicity study	0, 300, 1 000, 3 000 ppm	M: 30.5 F: 33.4
		M: 0, 10.5, 30.5, 99.6 F: 0, 9.4, 33.4, 104	M/F: Increased BUN and Cre
	Two-year chronic toxicity study	0, 200, 800, 4 000 ppm	M: 93.1 F: 18.5
		M: 0, 4.56, 19.0, 93.1 F: 0, 4.84, 18.5, 90.0	M: No toxicity was observed F: Suppressed body weight
ADI			NOAEL: 9.43 SF: 100 ADI: 0.094
The critical study for setting ADI			Two-generation reproductive toxicity study in rats

ADI: Acceptable daily intake, NOAEL: No-observed-adverse-effect level, SF: Safety factor
[1)] The adverse effect observed at LOAEL
[2)] Values are converted into the concentration of free base of kasugamycin