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

Risk Assessment Report

Azoxystrobin (6th edition)

(Pesticides and additives)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted the risk assessment of a strobilurin fungicide, azoxystrobin (CAS No. 131860-33-8), using results from various studies. A current application is a new use as post-harvest to potato. In the current assessment, the results of fate in animals (chicken), residue in livestock products (chicken) and 21-day subacute percutaneous toxicity (rats) were newly available.

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

Major adverse effects of azoxystrobin observed are suppressed body weight, anemia, common bile-duct dilatation and hyperplasia of bile duct epithelial cells. Azoxystrobin showed no neurotoxicity, carcinogenicity, effects on reproduction activity, teratogenicity and genotoxicity relevant to human health.

From the above results, FSCJ identified that the relevant substance for the residue definition for dietary risk assessment in agricultural products, livestock products and fishery products to be azoxystrobin (parent compound only).

The lowest value of the no-observed-adverse-effect level (NOAEL) in all tests was 18.2 mg/kg bw/day in combined two-year chronic toxicity/carcinogenicity study in rats. FSCJ specified an acceptable daily intake (ADI) of 0.18 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.[1]
The lowest NOAEL for potential adverse effects of a single oral administration of azoxystrobin was 150 mg/kg bw/day obtained in developmental toxicity studies in rabbits. FSCJ specified an acute reference dose (ARfD) to be 1.5 mg/kg bw by applying a safety factor of 100 to the NOAEL.

[1] This ADI was the same as the ADI reported in the 5th edition (2013).

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

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, 200, 2 000, 4 000[2)] ppm M: 0, 20.4, 211, 444 F: 0, 22.4, 223, 449	M: 20.4 F: 22.4	M: 211 F: 223	M/F: Suppressed body weight
	90-day subacute neurotoxicity study	0, 100, 500, 2 000 ppm M: 0, 8.0, 38.5, 161 F: 0, 9.1, 47.9, 202	M: 38.5 F: 47.9	M: 161 F: 202	M/F: Suppressed body weight (No neurotoxicity)
	Combined two-year chronic toxicity/carcinogenicity study	0, 60, 300, 750/1 500[3)] ppm M: 0, 3.6, 18.2, 82.4 F: 0, 4.5, 22.3, 117	M: 18.2 F: 22.3	M: 82.4 F: 117	M/F: Suppressed body weight (No carcinogenicity)
	Two-generation reproductive activity study	0, 60, 300, 1 500 ppm PM: 0, 6.5, 33.0, 162 PF: 0, 6.9, 34.4, 171 F_1M: 0, 6.3, 31.7, 168 F_1F: 0, 6.7, 33.2, 179	Parent: PM: 33.0 PF: 34.4 F_1M: 31.7 F_1F: 33.2 Offspring: PM: 33.0 PF: 34.4 F_1M: 31.7 F_1F: 33.2	Parent: PM: 162 PF: 171 F_1M: 168 F_1F: 179 Offspring: PM: 162 PF: 171 F_1M: 168 F_1F: 179	Parent: Suppressed body weight Offspring: Low body weight (No effect on reproductive activity)
	Developmental toxicity study	0, 25, 100, 300	Dams: 25 Fetuses: 25	Dams: 100 Fetuses: 100	Dams: Diarrhea Fetuses: Incontinence of urine, increase in delayed ossification (No teratogenicity)
Mouse	Two-year carcinogenicity study	0, 50, 300, 2 000 ppm M: 0, 6.2, 37.5, 272 F: 0, 8.5, 51.3, 363	M: 37.5 F: 51.3	M: 272 F: 363	M/F: Suppressed body weight (No carcinogenicity)

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Critical endpoints[1)]
Rabbit	Developmental toxicity study (the 1st study)	0, 50, 150, 500	Dams: - Fetuses:500	Dams: 50 Fetuses: -	Dams: Decrease in body weight Fetuses: No toxicity (No teratogenicity)
	Developmental toxicity study (the 2nd study) (Maternal toxicity)	0, 25, 40, 150	Dams: 25	Dams: 40	Dams: Low body weight, decreased feed consumption
Dog	90-day subacute toxicity study	0, 10, 50, 250 M: 0, 28.2, 144, 288 F: 0, 30.0, 147, 326	M: 10 F: 10	M: 50 F: 50	M: Hygrostomia, spitting and vomiting F: Suppressed body weight
	One-year chronic toxicity study	0, 3, 25, 200	M: 25 F: 25	M: 200 F: 200	M/F: Increased T. Chol. and TG
ADI			NOAEL: 18.2 mg/kg bw/day SF: 100 ADI: 0.18 mg/kg bw/day		
The critical study for setting ADI			Combined two-year chronic toxicity/carcinogenicity study in rats		

ADI: Acceptable daily Intake, NOAEL: No-observed-adverse-effect level, SF: Safety factor
-: NOAEL or LOAEL could not be specified

[1] The adverse effect observed at LOAEL
[2] Although the maximum dose at the beginning was 6 000 ppm, the dose was changed to 4 000 ppm from the third week since the animal growth was disrupted after two weeks.
[3] Although the maximum dose at the beginning was 1 5000 ppm, it was changed to 750 ppm from the 53rd week since incident of death increased and started spitting at 39th week after the beginning of treatment.

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

Species	Study	Dose (mg/kg bw/day)	Endpoints relevant to setting NOAEL and ARfD (mg/kg bw or mg/kg bw/day) [1]
Rat	Acute neurotoxicity study	M/F: 0, 200, 600, 2 000	M: 600 M: Suppressed body weight
Rabbit	Developmental toxicity study (the 1st study)	Dams: 0, 50, 150, 500	Dams: 150 Dams: Decreased body weight, decreased feed consumption
ARfD			NOAEL: 150 SF: 100 ARfD: 1.5
The critical study for setting ADI			Developmental toxicity study in rabbits (the 1st study)

ARfD, Acute reference dose; NOAEL, No-observed-adverse-effect level; SF: Safety factor
[1]The adverse effect observed at LOAEL