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

# Risk Assessment Report

## Oxazosulfyl

(Pesticides)

Food Safety Commission of Japan (FSCJ)
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## ABSTRACT

FSCJ conducted the risk assessment of an insecticide composed of a novel skeleton structure, oxazosulfyl (CAS No. 1616678-32-0), based on various documents.

The data used in the assessment include fate in animals (rats, goats and chicken), fate in plants (paddy rice), residues in plants, subacute toxicity (rats, mice and dogs), subacute neurotoxicity (rats), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproduction toxicity (rats), developmental toxicity (rats and rabbits), genotoxicity and data on inductions of metabolic enzyme of the liver

Major adverse effects of oxazosulfyl observed are suppressed body weight, hepatocellular hypertrophy, hypertrophy of follicular epithelial cells in the thyroid, and tremor. Oxazosulfyl showed no carcinogenicity, effects on reproduction activity, teratogenicity and genotoxicity.

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

The lowest value of the no-observed-adverse-effect level (NOAEL) in all tests was 5 mg/kg bw/day in a one-year chronic toxicity study in dogs. FSCJ specified an acceptable daily intake (ADI) of 0.05 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.
The lowest NOAEL or LOAEL for potential adverse effects of a single oral administration of oxazosulfyl was 25 mg/kg bw/day obtained in an acute neurotoxicity study in rats. FSCJ specified an acute reference dose (ARfD) to be 0.25 mg/kg bw by applying a safety factor of 100 to the NOAEL.

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

| 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, 150, 550, 2 000 ppm<br>M: 0, 9.42, 32.7, 116<br>F: 0, 11.0, 39.5, 129 | M: 32.7<br>F: 39.5 | M: 116<br>F: 129 | M/F: Diffuse hypertrophy of hepatocytes |
| | 90-day subacute neurotoxicity study | 0, 150, 550, 2 000 ppm<br>M: 0, 9.49, 35.2, 124<br>F: 0, 11.5, 41.3, 133 | M: 385.2<br>F: 41.3 | M: 124<br>F: 133 | M/F: Abnormal behavior and phonation, tremor |
| | Combined two-year chronic toxicity/carcinogenicity study | 0, 100, 300, 1 000(M), 1 000/600 (F) ppm<br>Carcinogenicity group:<br>M: 0, 3.87, 11.7, 40.5<br>F: 0, 4.93, 15.6, 45.2<br>One-year chronic toxicity group:<br>M: 0, 4.46, 13.6, 44.7<br>F: 0, 5.80, 18.7, 59.2 | M: 11.7<br>F: 15.6 | M: 40.5<br>F: 45.2 | M/F: Diffuse hypertrophy of hepatocytes<br><br>(No carcinogenicity) |
| | Two-generation reproduction activity study | 0, 50, 200, 700 ppm<br>PM: 0, 3.09, 12.3, 43.1<br>PF: 0, 3.77, 15.4, 53.4<br>$F_1$M: 0, 3.90, 15.5, 55.0<br>$F_1$F: 0, 4.38, 17.8, 63.6 | Parent:<br>PM: 12.3<br>PF: 15.4<br>$F_1$M: 15.5<br>$F_1$F: 17.8<br><br>Offspring:<br>PM: 12.3<br>PF: 15.4<br>$F_1$M: 15.5<br>$F_1$F: 17.8 | Parent:<br>PM: 43.1<br>PF: 53.4<br>$F_1$M: 55.0<br>$F_1$F: 63.6<br><br>Offspring:<br>PM: 43.1<br>PF: 53.4<br>$F_1$M: 55.0<br>$F_1$F: 63.6 | Parent: Suppressed body weight, decreased feed consumption<br><br>Offspring: Suppressed body weight<br><br>(No effect on reproductive activity) |
| | Developmental toxicity study | 0, 6, 20, 60 | Dams: 20<br>Fetuses: 60 | Dams: 60<br>Fetuses: - | Dams: Suppressed body weight, decreased feed consumption<br>Fetuses: No toxicity<br><br>(No teratogenicity) |
| Mouse | 90-day subacute toxicity study | 0, 1 750, 3 500, 7 000 ppm<br>M: 0, 229, 464, 894<br>F: 0, 267, 509, 939 | M: 229<br>F: 267 | M: 464<br>F: 509 | M/F: Abnormal phonation |
| | 18-month carcinogenicity study | 0, 70, 700, 7 000/5 000 ppm<br>Carcinogenicity group:<br>M: 0, 7.51, 76.9, 770<br>F: 0, 7.27, 74.0, 730<br>One-year chronic toxicity group: | M: 76.9<br>F: 74.0 | M: 770<br>F: 730 | M/F: Centrilobular hypertrophy of hepatocytes, hypertrophy of follicular epithelial cells in the thyroid |

| Species | Study | Dose (mg/kg bw/day) | NOAEL (mg/kg bw/day) | LOAEL (mg/kg bw/day) | Critical endpoints[1] |
|---|---|---|---|---|---|
| | | M: 0, 8.01, 79.2, 833<br>F: 0, 7.84, 80.5, 793 | | | (No carcinogenicity) |
| Rabbit | Developmental toxicity study | 0, 2, 6, 20 | Dams: 6<br>Fetuses: 6 | Dams: 20<br>Fetuses: 20 | Dams: Suppressed body weight<br>Fetuses: Low body weight<br><br>(No teratogenicity) |
| Dog | 90-day subacute toxicity study | 0, 3, 10, 50, 150 (M), 150/100 (F) | M: 3<br>F: 10 | M: 10<br>F: 50 | M/F: Increased ALP, Centrilobular hypertrophy of hepatocytes |
| | One-year chronic toxicity study | 0, 1, 5, 30 | M/F: 5 | M/F: 30 | M/F: Increased GGT, Centrilobular hypertrophy of hepatocytes |
| ADI | | | NOAEL: 5<br>SF: 100<br>ADI: 0.05 | | |
| The critical study for setting ADI | | | One-year chronic toxicity study in dogs | | |

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

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

| 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 toxicity study | 300, 2 000 | F: -<br><br>F: Tremor, abnormal phonation, mydriasis |
| | Acute neurotoxicity study | 0, 25, 200, 400 | M/F: 25<br><br>M/F: Decreased body temperature, decreased locomotor activity |
| ARfD | | | NOAEL: 25<br>SF: 100<br>ARfD: 0.25 |
| The critical study for setting ADI | | | Acute neurotoxicity study in rats |

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