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

# Risk Assessment Report

## Acrinathrin

(Pesticides)

Food Safety Commission of Japan (FSCJ)
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## ABSTRACT

FSCJ conducted a risk assessment of acrinathrin (CAS No.101007-06-1), a pyrethroid insecticide, based on results from various studies.

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

Major adverse effects of acrinathrin observed are suppressed body weight, decreased feed consumption, and scab-formation. Effects on the reproductivity, teratogenicity and genotoxicity relevant to human health were not observed.

Increases in the incidence of benign granulosa- theca cell tumors were observed in the ovary in rats in a two-year combined chronic toxicity/carcinogenicity study. However, a genotoxic mechanism was unlikely to be involved in the tumor development. It was thus considered possible to establish a threshold in the assessment.

Based on the results from various studies, acrinathrin (only parent compound) was identified as the relevant substance for the residue definition for dietary risk assessment in agricultural products.

The lowest no-observed-adverse-effect level (NOAEL) obtained in all studies was 1.61 mg/kg bw/day in a two-year combined chronic toxicity/carcinogenicity study in rats. FSCJ specified an acceptable daily intake (ADI) of 0.016 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.
The lowest NOAEL for adverse effects which is likely elicited by a single oral administration of acrinathrin was 3 mg/kg bw obtained in an acute neurotoxicity study in rats. FSCJ specified an acute reference dose (ARfD) to be 0.03 mg/kg bw by applying a safety factor of 100 to the NOAEL.

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

| Species | Study | Dose (mg/kgbw/day) | NOAEL[1)] (mg/kg bw/day) |
|---|---|---|---|
| Rat | 90-day subacute toxicity study (the 1st study) | 0, 30, 100, 300 ppm<br>M: 0, 2.4, 8.0, 24.3<br>F: 0, 3.1, 10.2, 30.5 | M: 2.4<br>F: 3.1<br>M/F: Skin lesions |
| | 90-day subacute toxicity study (the 2nd study) | 0, 30, 100, 300, 1 000 ppm<br>M: 0, 2.58, 9.05, 26.6, 89.4<br>F: 0, 3.04, 10.1, 27.9, 93.7 | M: 2.58<br>F: 3.04<br>M/F: Crust or abrasion |
| | 90-day subacute neurotoxicity study | 0, 30, 150, 750 ppm<br>M: 0, 2.4, 12.6, 62.6<br>F: 0, 2.9, 14.4, 67.6 | (General toxicity)<br>M: 2.4<br>F: 2.9<br>M/F: Suppressed body weight<br>(Neurotoxicity)<br>M: 2.4<br>F: No neutotoxicity<br>M: Decreased grip strength of forelimb and hindlimb |
| | Two-year combined chronic toxicity /carcinogenicity study (the 1st study) | 0, 30, 300, 150, 750 ppm<br>M: 0, 1.61, 8.13, 42.7<br>F: 0, 2.01, 10.3, 53.9 | M: 1.61<br>F: 2.01<br>M/F: Suppressed body weight and decreased food consumption<br>F: Increases in the incidence of benign granulosa-theca cell tumor in the ovary |
| | Two-generation reproductive toxicity study | 0, 5, 20, 80 ppm<br>PM:0, 0.57, 2.2, 9.0<br>PF: 0, 0.66, 2.6, 10.0<br>F1M: 0, 0.67, 2.6, 9.5<br>F1F: 0, 0.76, 3.0, 11.0 | (Parent)<br>PM: 0.57<br>PF: 0.66<br>$F_1$M: 0.67<br>$F_1$F: 0.76<br>(Offspring)<br>PM: 9.0<br>PF: 10.0<br>$F_1$M: 9.5<br>$F_1$F: 11.0<br>Parent: Skin lesions<br>Offspring: No toxicity was observed<br>No effect on reproduction |

| | | | |
|---|---|---|---|
| | Developmental toxicity study | 0, 2, 6, 18 | Dams: 2<br>Fetuses: 6<br><br>Dams: Decrease in body weight/ Suppressed body weight<br>Fetuses: A decrease in the survival rate Lower body weight<br><br>(No teratogenicity) |
| Mouse | 90-day subacute toxicity study | 0, 30, 100, 300, 1 000 ppm | M: 4.27<br>F: 5.31<br><br>M/F: Crust or abrasion |
| | | M: 0, 4.27, 14.3, 39.0, 143<br>F: 0, 5.31, 21.1, 60.1, 204 | |
| | 18-month carcinogenicity study (the 1st study) | 0, 3, 15, 75 ppm | M: 2.49<br>F: 3.00<br><br>M/F: Skin lesions<br><br>(No carcinogenicity) |
| | | M: 0, 0.51, 2.49, 13.1<br>F:0, 0.59, 3.00, 15.0 | |
| | 18-month carcinogenicity study (the 2nd study) | 0, 30, 150, 750 ppm | M: 4.0<br>F: 5.1<br><br>M/F: Suppressed body weight, skin lesions<br><br>(No carcinogenicity)<br><br>Enhanced activity of blood and Lymphoreticular System |
| | | M: 0, 4.0, 21.0, 109<br>F: 0, 5.1, 25.5, 141 | |
| Rabbit | Developmental toxicity study | 0, 15, 45, 135 | Dams: 15<br>Fetuses: 45<br><br>Dams: Decrease in body weight/ Suppressed body weight<br>Fetuses: A decrease in the survival rate |
| Dog | 90-day subacute toxicity study | 0, 1, 3, 10 | M/F: 3<br><br>M/F: Decrease in body weight |
| | One-year chronic toxicity study | 0, 1, 3, 10 | M/F: 3<br><br>M/F: Decrease in body weight/Suppressed body weight |
| ADI | | | NOAEL: 1.61<br>SF: 100<br>ADI: 0.016 |
| The critical study for setting ADI | | | Rat: Two-year combined chronic toxicity/ carcinogenicity study (the 1st study) |

ADI, Acceptable daily intake; SF, Safety factor; NOAEL, No-observed-adverse-effect level
[1)], The adverse effect observed at LOAEL

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

| 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 study | M/F: 5 000 | –<br>M/F: Sedation and piloerection |
| | Acute neurotoxicity study | M/F: 0, 1, 3, 10, 37.5 | M/F: 34<br>M: Decrease in body temperature<br>F: Suppressed body weight |
| | Developmental toxicity study | 0, 2, 6, 18 | Dams: 6<br>Dams: Suppressed body weight |
| Mouse | Acute toxicity study | M/F: 5 000 | –<br>M/F: Sedation and ptosis |
| | General pharmacology (Central nervous system) | M/F: 0, 375, 750, 1 500, 3 000, 6 000 | M/F: 750<br>M/F: Decrease in body temperature |
| Rabbit | Developmental toxicity study | 0, 15, 45, 135 | Dams: 45<br>Dams: Decrease in body weight/suppressed body weight |
| ARfD | | | NOAEL: 3<br>SF: 100<br>ARfD: 0.03 |
| The critical study for setting ARfD | | | Acute neurotoxicity study in rats |

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