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

Risk Assessment Report

Triflumizole

(Pesticides)

Food Safety Commission of Japan (FSCJ)

November 2013

ABSTRACT

FSCJ conducted a risk assessment of "triflumizole" (CAS No.68694-11-1), an imidazole fungicide, based on summary reports made by applicants and other documents.

The data used in the assessment were on: fate in animals (rats), fate in plants (cucumbers, pears, etc.), residues in crops, subacute toxicity (rats and mice), chronic toxicity (dogs, including 13 week interim sacrifice group), combined chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), reproductive toxicity (rats), developmental toxicity (rats and rabbits), genotoxicity, etc.
Major adverse effects of triflumizole observed were: decreased body weight gain and hepatocellular hypertrophy and others in the liver.

No carcinogenicity, teratogenicity or genotoxicity was observed.

Decreased activity and decreased stereotyped behavior were observed in the acute neurotoxicity study in rats, but no neurotoxicity was observed in the 90-day subacute neurotoxicity study in rats.

In the reproductive toxicity study and developmental toxicity study in rats, an increase in placental weights was observed. In special studies on the mode of action, a decreased tendency of circulating estradiol concentration and an increase in testosterone levels were observed. These effects may be attributable to aromatase inhibition, which is often caused by imidazole fungicides.

Based on various study results, only triflumizole (parent compound) was included in the residue definition for dietary risk assessment in agricultural products and fishery products.

Among the NOAELs and LOAELs obtained in various studies, the lowest value was 3.7 mg/kg bw/day, which was the NOAEL obtained in a two-year combined chronic toxicity/carcinogenicity study in male rats. Based on this value and applying a safety factor of 100, an acceptable daily intake (ADI) was calculated to be 0.037 mg/kg bw/day. Meanwhile, in a two-year combined chronic toxicity/carcinogenicity study, a NOAEL could not be obtained for female rats, and the LOAEL was 4.6 mg/kg bw/day. Since hepatotoxicity observed at this LOAEL was weak, an additional safety factor of 3 was considered appropriate to specify the ADI based on this LOAEL. Consequently the ADI using this LOAEL was calculated to be 0.015 mg/kg bw/day.
Since this value is lower than the value (0.037 mg/kg bw/day) obtained for male rats in the two-year combined chronic toxicity/carcinogenicity study, FSCJ considered it appropriate to specify the ADI using the LOAEL obtained for females in the two-year combined chronic toxicity/carcinogenicity study in female rats.

Consequently, FSCJ specified the ADI for triflumizole at 0.015 mg/kg bw/day, based on the LOAEL (4.6 mg/kg bw/day) obtained for females in the two-year combined chronic toxicity/carcinogenicity study and applying a safety factor of 300 (10 for species difference, 10 for individual difference, and 3 for the adopted LOAEL value).