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

Risk Assessment Report

Procymidone

(Pesticides)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted a risk assessment of procymidone (CAS No. 32809-16-8), a dicarboximide fungicide, based on summary reports made by applicants and documents of EU, JMPR and others

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

Major adverse effects of procymidone observed are: hepatocellular hypertrophy and others in the liver, and interstitial cell hyperplasia in the testis. No genotoxicity was observed.

In the carcinogenicity studies in rats, an increase in the incidence of testicular interstitial cell tumors was observed. The studies on the mechanism for the carcinogenicity revealed that procymidone has a binding activity to androgen receptors (AR) and thus results in unbalance in the blood hormones (increase in LH).

Therefore, incidence of testicular interstitial cell tumors was likely to be a consequence of prolonged stimulation with the increased LH. In addition, incidence of hepatoblastomas tended to increase in male mice. However, the mechanism for the tumor development was hardly attributable to genotoxicity, thus FSCJ concluded that it was possible to establish a threshold dose in the assessment.

In the reproduction test and developmental toxicity study, aberration of the genitals (shortened distance between anus and external urethral orifice, hypospadias and others) and a decrease in male reproductive rate were observed. However, similar effects were not observed in fetuses of rabbits and monkeys. From studies on species difference, the major factor of the species difference was suggested to be the fact that the serum concentration of the hydroxide, a major metabolite, is kept at higher in the enterohepatic circulation in rats.

Based on the results from various studies, FSCJ specified the residue definition for this dietary risk assessment in agricultural products to be procymidone (parent compound only).

The minimum value of the no observed adverse effect level (NOAEL) obtained in all tests was 3.5 mg/kg bw/day obtained in a developmental toxicity study in rats. FSCJ specified an acceptable daily intake (ADI) of 0.035 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.