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

Risk Assessment Report

Hexythiazox

(Pesticides)

Food Safety Commission of Japan (FSCJ)
March 2015

ABSTRACT

FSCJ conducted a risk assessment of hexythiazox (CAS No. 78587-05-0), an arcaricide based on the summary report made by applicants and documents from JMPR, Government of the US and EU.

The studies include the fate in animals (rats, goats and chicken), fate in plants (oranges pears and others), residues in crops, subacute toxicity (rats and mice), subacute neurotoxicity (rats), chronic toxicity (dogs), combined chronic toxicity/carcinogenicity (rats and mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits) and genotoxicity.

Major adverse effects of hexythiadox observed are decreased body weight gain, hepatocellular hypertrophy and increased organ weights in the liver; vacuolation of the adrenal cortex, increased organ weights in the adrenal glands. No neurotoxicity, developmental toxicity, teratogenicity or genotoxicity was observed.

Increases in the incidence of hepatocellular adenomas and total incidences of hepatocellular adenomas and carcinomas, as well as hepatoblastomas were observed in female mice and increased trend in the total incidences of hepatocellular adenomas, carcinomas, and hepatobalastomas were observed in male mice in a two-year combined chronic toxicity/carcinogenicity study. However, a genotoxic mechanism was unlikely to be involved in the tumor induction. It was thus considered possible to establish a threshold dose in the assessment.

Based on the above results, only hexythiazox (parent compound) or hexythiazox and a metabolite which has the same chemical structure as metabolite [I] were identified as the residue definition for dietary risk assessment in the agricultural products or livestock products, respectively.

The lowest no-observed-adverse-effect level (NOAEL) obtained in all tests was 2.87 mg/kg bw/day in a one-year chronic toxicity study in dogs. Applying a safety factor of 100 to the NOAEL, FSCJ specified an acceptable daily intake (ADI) of 0.028 mg/kg bw/day.

The lowest NOAEL for potential adverse effects of a single oral administration of hexythiazox was 720 mg/kg bw/day in a developmental toxicity study in rats. FSCJ considered it unnecessary to specify an acute reference dose (ARfD), since the NOAEL was above the cut-off level (500 mg/kg bw).