

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

Risk Assessment Report

Metrafenone (Pesticides)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted a risk assessment of metrafenone (CAS No. 220899-03-6), a benzophenone fungicide, based on results from various studies.

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

Major adverse effects of metrafenone observed are increased organ weights in the kidney, centrilobular necrosis of hepatocytes, and interstitial nephritis/chronic progressive nephrosis in the kidney. No neurotoxicity, developmental toxicity, teratogenicity, immunotoxicity or genotoxicity was observed.

Increases in the incidence of hepatocellular adenomas was observed in rats in a two-year combined chronic toxicity/carcinogenicity study. In addition, increases in the incidence of hepatocellular adenomas and total incidences of hepatocellular adenomas and carcinomas were observed in mice in an 18-month carcinogenicity study, but 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 metrafenone (parent compound) was identified as the residue definition for dietary risk assessment in the agricultural products.

The lowest no-observed-adverse-effect level (NOAEL) obtained in all tests was 24.9 mg/kg bw/day in a two-year combined chronic toxicity/carcinogenicity study in rats. Applying a safety factor of 100 to the NOAEL, FSCJ specified an acceptable daily intake (ADI) of 0.24 mg/kg bw/day.

FSCJ considered it unnecessary to specify an acute reference dose (ARfD), since it is unlikely that metrafenone exerts toxic effects after a single dose administration.