

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

Risk Assessment Report

Thiabendazole

(Pesticides)

Food Safety Commission of Japan (FSCJ)

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ABSTRACT

FSCJ conducted a risk assessment of thiabendazole (CAS No. 149-79-8), a heterocyclic fungicide, based on materials including documents from the Joint FAO/WHO Meeting on Pesticide Residues (JMPR), the Joint FAO/WHO Expert Committee on Food Additives (JECFA), and the governments of EU and the US.

The data used in the assessment include fate in animals (rats, mice, dogs and livestock), fate in plants (wheat and soybean), residues in crops, subacute toxicity (rats and dogs), chronic toxicity (rats and dogs), carcinogenicity (rats and mice), two-generation reproductive toxicity (rats), developmental toxicity (rats, mice and rabbits) and genotoxicity.

Major adverse effects of thiabendazole observed are hepatocellular hypertrophy in the liver, hyperplasia of thyroid follicular cells, hyperplasia of transitional epithelia of the renal pelvis, and effects on blood such as anemia. No reproductive toxicity was observed. Genotoxicity tests showed aneuploidy characterized by an abnormal number of chromosomes, but it was possible to set a threshold value.

Significant increases in the incidences of follicular thyroid adenomas and preputial gland adenomas were observed in a carcinogenicity study in rats. However, a genotoxic mechanism was unlikely to be involved in the tumor induction. Even if a genotoxic mechanism is involved in the tumor induction, the relevant mechanism is attributable to the aneuploidy resulting from the inhibition of tubulin polymerization. It was thus considered possible to establish a threshold in the assessment.

Developmental toxicity tests in rabbits showed that thiabendazole at the dose with maternal toxicity caused a significant increase in developmental malformations in fetuses. No effect on teratogenicity was observed in rats.

Based on the above results, thiabendazole (parent compound) was identified as the residue definition for dietary risk assessment in agricultural products, and thiabendazole and its metabolite H were for livestock products.

The lowest no-observed-adverse-effect level (NOAEL) in the toxicological studies was 10 mg/kg bw/day in a one-year chronic toxicity study in dogs, a two-year combined chronic toxicity/carcinogenicity study and a two-generation reproductive toxicity study in rats, taking into account the difference in the common ratio of doses used in each study. Applying a safety factor of 100 to the NOAEL, FSCJ specified the acceptable daily intake (ADI) to be 0.1 mg/kg bw/day.