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

Risk Assessment Report

Triforine

(Pesticides)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted a risk assessment of a piperazine fungicide, triforine (CAS No. 26644-46-2), based on results from various studies and assessment reports bynational/international organizations.

The data used in the assessment include fate in animals (rats, sheep and chiken), fate in plants (tomatoes and apples,), residues in crops, subacute toxicity (rats, mice and dogs), combind subacute toxicity/neurotoxicity (rats), chronic toxicity (rats and dogs), combind chronic toxicity/carcinogenicity (rats), carcinogenicity (mice), two-generation reproductive toxicity (rats), developmental toxicity (rats and rabbits), immunotoxicity (rats and mice) ,genotoxicity, and on enzyme induction in the liver.

Major adverse effects of triforine observed are suppressed body weight and hematological effects such as anemia. Triforine showed no neurotoxicity, adverse effects on reproductivity, teratogenicity, immunotoxicity and genotoxicity relevant to human health.
An incidence of alveolar-bronchiolar adenomas and a combined incidence in bronchiolo-alveolar adenomas and adenocarcinomas were increased by the treatment in female mice in a 105-weeks carcinogenicity study. However, a genotoxic mechanism was unlikely to be involved in the tumor development. It was thus considered possible to establish a threshold in the assessment.

Based on the results from various studies, only triforine (parent compound only) was identified as the residue definition for dietary risk assessment in agricultural products and livestock products.

The lowest no-observed-adverse-effect level (NOAEL) obtained in all tests was 2.39 mg/kg bw/day in a 2-years chronic toxicity study in dogs. FSCJ specified an acceptable daily intake (ADI) of 0.023 mg/kg bw/day by applying a safety factor of 100 to the NOAEL.
The lowest NOAEL for potential adverse effects of single oral administration of triforine was 150 mg/kg bw obtained from the combined evaluation in two developmental toxicity studies (Studies No. 2 and No.3) in rabbits. FSCJ specified an acute reference dose (ARfD) to be 1.5 mg/kg bw by applying a safety factor of 100 to this value.