

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

Risk Assessment Report

Cymoxanil (Pesticides)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted a risk assessment of cymoxanil (CAS No. 57966-95-7), a cyanoacetamide fungicide, based on results of various studies.

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

Major adverse effects of cymoxanil were observed in the testis (atrophy and elongated spermatid degeneration, as well as oligospermia in dogs), epididymis (atrophy, increase in multinucleated spermatid cells and sperm granulomas), thymus (decreased weights and atrophy in dogs), and eye (retinal atrophy). No carcinogenicity, developmental neurotoxicity, immunotoxicity, and genotoxicity relevant to human health were observed.

A two-year combined chronic toxicity/carcinogenicity study in rats exhibited increased hyperactivity and aggressiveness as well as retinal atrophy in male rats of the middle and high dose groups and increased incidence of sciatic nerve axon/myelin degeneration in female rats of the same dose group.

A two-generation reproduction study in rats showed decreased mean number of corpora lutea and mean number of implantations in the high dose group. Developmental toxicity study revealed hypoplasia of sternbra as well as dilation of the renal pelvis in rats, and dilation of the ventricles of the heart, dilation of the renal pelvis as well as cleft palate in rabbits.

Based on the above results, only cymoxanil (parent compound) was identified as the residue definition for dietary risk assessment in agricultural products.

The lowest dose of no-observed-adverse-effect level (NOAEL) and low-observed-adverse-effect level (LOAEL) in the toxicological studies was the NOAEL of 1.3 mg/kg bw/day in a one-year chronic toxicity study in male dogs. Applying the safety factor of 100 to the NOAEL, FSCJ specified an acceptable daily intake (ADI) to be 0.013 mg/kg bw/day.

The lowest NOAEL for potential adverse effects of a single oral administration of cymoxanil was 8 mg/kg bw/day in a developmental toxicity study in rats, which was close to the lowest NOAEL of 8.25 mg/kg bw/day in a 90-day repeated dose toxicity study in mice.

Based on the results, applying the safety factor of 100 to the NOAEL of 8 mg/kg bw/day in a developmental toxicity study in rats, FSCJ specified the acute reference dose (ARfD) to be 0.08 mg/kg bw.