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

Risk Assessment Report

Thymol

(Veterinary Medicinal Products)

Food Safety Commission of Japan (FSCJ)
April 2018

ABSTRACT

FSCJ conducted a risk assessment of a paraciticide, thymol (CAS No. 89-83-8), based on a written application for the marketing approval of new veterinary medicinal products.

Data used in the assessment include pharmacokinetics (rats, rabbits, dogs and humans), residues (honey bees), genotoxicity, acute toxicity (mice, rats, guinea pigs, and rabbits), subacute toxicity (rats), and reproductive and developmental toxicities (rats).

Major adverse effects of thymol observed are a tendency of transiently suppressed body weight in male rats, and a transiently decreased motor activity and ataxic gait in female rats.
FSCJ judged that thymol has no genotoxicity relevant to human health based on the data of all genotoxicity studies. Therefore, FSCJ concluded that the acceptable daily intake (ADI) for thymol could be specified.

The effects observed at the lowest dose in various toxicological studies were a tendency of transiently suppressed body weight in male rats, and a transiently decreased motor activity and ataxic gait in female rats in a 43-day subacute toxicity study in rats, and low body weight and low body weight gain in offsprings in one-generation reproductive and developmental toxicity study in rats. The lowest no-observed-adverse-effect level (NOAEL) in these studies was 40 mg/kg body weight/day.

There were no data of carcinogenicity, however FSCJ recognized that the adverse effects observed in the toxicity studies were transient and not serious. The risk assessments by JECFA, Europe and U.S. have concluded that specification of ADI and MRL for thymol was unnecessary. Considering these and a long xeperience of use as a food additive or na additive in medicinal products in humans, FSCJ concluded that it is not necessary to specify an ADI for thymol as long as it is used appropriately as veterinary medicinal products.

Table 1. *Levels relevant to toxicological evaluation of thymol*

Species	Study	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day) and Critical endpoints[1]
Rats	28-day subacute toxicity study	15.39, 30.78, 61.55 (gavage administration)	61.55 No adverse effect was observed
	43-day subacute toxicity study	8, 40, 200 (gavage administration)	M : 40 A tendency of transiently suppressed body weight F : 40 A transiently decreased motor activity and ataxic gait
	19-week subacute toxicity study	75, 750* (dietary administration)	750 No adverse effect was observed
	One-generation reproductive and developmental toxicity study	8, 40, 200 (gavage administration)	Parents: 200 Offspring: 40 Low body weight, and low body weight gain
Toxicological ADI			It is unnecessary to specify an ADI for thymol as lon as it is used appropriately as a veterinary medicinal product.
The critical study for setting ADI			43-day subacute toxicity study in rats, and One-generation reproductive developmental toxicity study
ADI			-

*; Dietary concentration at 1000 or 10,000 equivalent to 75 or 750 mg/kg bw/day

[1] Major adverse effect observed at LOAEL