

7. *Metabolite toxicology.* There are no metabolites of toxicological significance to mammals.

8. *Endocrine disruption.* Chronic, lifespan, and multi-generational bioassays in mammals and acute and subchronic studies on aquatic organisms and wildlife did not reveal endocrine effects. Any endocrine-related effects would have been detected in this definitive array of required tests. The probability of any such effect due to agricultural uses of cymoxanil is negligible.

C. Aggregate Exposure

1. *Dietary exposure.* Cymoxanil is a fungicide currently registered in the United States for use on potatoes. In addition, tolerances have been for cymoxanil on imported tomatoes and

grapes. This tolerance petition proposes the following new uses in the United States: Cucurbit vegetables, fruiting vegetables and head lettuce. There are no residential uses.

i. *Food—a. Chronic dietary exposure assessment.* The chronic RfD of 0.041 mg/kg/day is based on a NOEL of 4.08 mg/kg/day from the 1 year rat feeding study and an uncertainty factor of 100. The acute NOEL of 4.0 mg/kg/day is based upon maternal clinical signs and weight effects at higher levels in a rat developmental study.

Chronic dietary cymoxanil exposure risks resulting from the proposed use of DPX-KP481 50DF on cucurbits, fruiting vegetables, head lettuce, potatoes and imported grapes were estimated using the Dietary Exposure Evaluation Model (DEEM, Novigen Sciences, Inc., 1999

Version 6.74). The analysis conservatively assumed that 30% of the crops on the proposed label would be treated with DPX-KP481 50DF and used field trial residue data. The chronic dietary risk estimate for cymoxanil shows that an adequate margin of safety exists for all population subgroups and that no effects would result from dietary exposure to cymoxanil.

The following table presents the analysis which indicate large margins of safety for each population subgroup and very low probability of effects resulting from chronic exposure to cymoxanil in DPX-KP481 50DF. No sensitive subpopulations were identified. For the general populations and all subpopulations 0.2% or less of the chronic RfD used.

TABLE 3.—RESULTS OF CHRONIC DIETARY ANALYSIS WITH CYMOXANIL

Population Group	Maximum Dietary Exposure (mg/kg/day)	% RfD
U.S. population	0.000063	0.2
Non-nursing infants (<1 yr.)	0.000016	<0.1
Children (1–6 yr.)	0.000074	0.2
Children (7–12 yr.)	0.000068	0.2
Females (13+)	0.000074	0.2

b. *Acute dietary exposure.* Results of the Tier 3 acute dietary exposure analysis show that an adequate margin of safety exists for all population subgroups and that no acute effects would result from dietary exposure to cymoxanil. The analysis conservatively assumed that 30% of the crops on the proposed label would be treated with DPX-KP481 50DF and used field trial residue data.

The results of the acute dietary exposure analysis for cymoxanil are given in the table below. The percentages of acute reference dose (aRfD) for cymoxanil were calculated based on an acute NOEL of 4 mg/kg/day from the rabbit developmental study based on maternal clinical signs and weight effects at the higher levels and an uncertainty factor of 100. The results of the acute dietary exposure analysis for cymoxanil indicate that the

predicted exposures, expressed as a percentage of the aRfD are well below 100%, showing cymoxanil clearly meets the Food Quality Protection Act (FQPA) standard of reasonable certainty of no harm and presents much lower acute dietary risk than many of its competitors. At the 99.9th percentile, the percentage of the aRfD was 4.47% for the general population and 5.72% for the most sensitive subpopulation, nursing females.

TABLE 4.—RESULTS OF ACUTE DIETARY ANALYSIS WITH CYMOXANIL

Population Group	99 th Percentile of Exposure		99 th Percentile of Exposure	
	Exposure (mg/kg/day)	%aRfD	Exposure (mg/kg/day)	%aRfD
U.S. population	0.000475	1.19	0.001789	4.47
Non-nursing infants (<1 yr.)	0.000184	0.46	0.000599	1.50
Children (1–6 yr.)	0.000576	1.44	0.002096	5.24
Children (7–12 yr.)	0.000485	1.21	0.001936	4.84
Females (13+ nursing)	0.000635	1.59	0.002287	5.72

ii. *Drinking water.* Surface water exposure was estimated using the

Generic Expected Environmental Concentration (GENEEC) model. Ground

water exposure was estimated using SCI-GROW. These are screening level