

levels as in the carcinogenicity study. A body weight gain depression of 10–11% in males and 14–22% in females with an accompanying decrease in food efficiency was observed at the high dose. The only other effect observed was a decrease in serum alkaline phosphatase in both sexes at the high dose and decreased alanine aminotransferase in high dose males. There was no evidence that pyraclostrobin produced a carcinogenic effect in rats. The NOAEL for the chronic rat and the cancer rat study is 75 ppm (ca. 3.4 mg/kg bwt/day males; 4.6 mg/kg bwt/day females).

Pyraclostrobin was administered to groups of 50 male and 50 female B6C3F1 mice at dietary concentrations of 0, 10, 30, 120 and 180 ppm (females only) for 18 months. Body weights were reduced at the HDT in both males and females. At the high dose, body weight gain decreases of 27% in females and 29% in males with an accompanying decrease in food efficiency were observed. No other signs of toxicity were noted at any dose level. The NOAEL was found to be 120 ppm (ca. 20.5 mg/kg bwt/day) for females and 30 ppm (ca. 4.1 mg/kg bwt/day) for males. There was no evidence that pyraclostrobin produced a carcinogenic effect in mice.

6. *Animal metabolism.* In a rat metabolism study with pyraclostrobin, 10–13% of the administered dose was excreted in the urine and 74–91% in the feces within 48 hours. Excretion via bile was significant accounting for 35–38% of the administered dose. By 120 hours after dosing, very little radioactivity remained in tissues. Pyraclostrobin was rapidly and almost completely

metabolized. Very little unchanged parent was detected. The phase one biotransformation is characterized by N-demethoxylation, various hydroxylations, cleavage of the ether bond and further oxidation of the two resulting molecule parts. Conjugation of the formed hydroxyl groups by glucuronic acid or sulfate also occurred. In summary, pyraclostrobin is extensively metabolized and rapidly eliminated primarily via the bile, with no evidence of accumulation in tissues.

7. *Metabolite toxicology.* A comparison of the rat metabolism results with the plant metabolism/residue results indicates that toxicology studies performed with the parent pyraclostrobin are sufficient to cover dietary exposure. Plant residues are primarily the parent compound with a fraction (up to 10–20% at most) being the demethoxylated parent. This metabolite is referred to as BF 500–3 in the plant studies and as 500M07 in the rat study. This metabolite in the rat is the first step in the major biotransformation process leading to the majority of the metabolites determined in the major excretion pathway.

8. *Endocrine disruption.* No specific test has been conducted with pyraclostrobin to determine whether the chemical may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen or other endocrine effects. However, there were no significant findings in other relevant toxicity studies (i.e., subchronic and chronic toxicity, teratology and multi-generation reproductive studies) which would suggest that pyraclostrobin produces endocrine related effects.

C. Aggregate Exposure

1. *Dietary exposure—i. Food Assessments* were conducted to evaluate the potential risk due to chronic and acute dietary exposure of the U.S. population to residues of pyraclostrobin (BAS 500 F). This fungicide and its desmethoxy metabolite (BAS 500-3) were expressed as the parent compound (BAS 500 F). Tolerance values have previously been established for various cereals, vegetables, fruits, and animal products and are listed in the U.S. EPA final rule published in the **Federal Register** September 27, 2002 (Vol 67, No. 188, p 60886 60902). This analysis included brassica (head & stem), lettuce (head & leaf), and leaves of root and tuber vegetables as the target crops.

The dietary assessment analysis followed an initial tier approach with only one refinement. Default processing factors, 100% crop treated, and anticipated residue values from the raw agricultural commodity (RAC) field studies along with some residue tolerances were assumed in the assessment. The CARES 1.1 model with the CSFII/FCID consumption data were used to calculate acute and chronic exposure estimates.

Acute dietary exposure. The estimated acute dietary exposure estimates for the crops listed were well under 100% of the aPAD at the 95th percentile (Table 2). The overall general population and the most sensitive subpopulation (females 13–49 years) utilized < 0.15% and 7.8% of the aRfD, respectively. The %aPAD ranged from 0.1 to 22.9% for all subpopulations.

Population	Exposure Estimate	%aRfD	%aPAD
Subgroups	(mg/kg bwt/day)		
Birth to 1 year	>0.00045	>.02	>.02
1–2 years	0.003053	0.10	0.10
3–5 years	0.003297	0.11	0.11
1–6 years	0.003215	0.11	0.11
6–12 years	0.002884	0.10	0.10
13–19 years	0.002515	0.08	0.08
Females 13–49 years	0.003888	7.78	22.87
Males 20–49 years	0.003405	0.11	0.11

Chronic: Results of the chronic dietary exposure assessments are listed below. The estimated chronic dietary

exposure from the crops listed above was less than 5.5% and 16.5% of the

cRfD and cPAD for all subpopulations, respectively.