

PERCENTAGES OF REFERENCE DOSE FOR CHRONIC EXPOSURE TO BAS 510 F

	U.S. Population (% of RfD)	Children 1–6 (% of RfD)
Chronic dietary exposure	34.0	77.1
Remainder of RfD available for water (%) (Drinking Water Level of Concern)	66.0	22.9
SCIGROW ground water estimation ¹	0.015	0.044
FIRST surface water estimation ¹	0.08	0.24
Total of RfD used by diet and water	34.1	77.4

¹ Used highest values predicted from the model for all agricultural uses; assumes 2L/day and 60 kg for adult; 1L/day and 10 kg for child

Overall, using worst-case parameters the predicted aggregate exposure by all potential routes for both adults and children is less than the chronic reference dose.

2. *Non-dietary exposure.* BAS 510 F is not currently planned for residential uses. Thus, residential exposure is not aggregated into the risk assessment.

D. Cumulative Effects

Section 408(b)(2)(D)(v) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider “available information” concerning the cumulative effects of a particular pesticide’s residues and “other substances that have a common mechanism of toxicity.” BAS 510 F is a foliar fungicide chemically belonging to the carboxin class of fungicides. BAS 510 F acts in the fungal cell by inhibiting mitochondrial respiration through inhibition of the succinate-ubiquinone oxidase reductase system in Complex II of the mitochondrial electron transport chain. BAS 510 F shares this mode of action with only one other currently registered U.S. pesticide - carboxin.

The EPA is currently developing methodology to perform cumulative risk assessments. At this time, there is no available data to determine whether BAS 510 F has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, BAS 510 F does not appear to produce a toxic metabolite produced by other substances.

E. Safety Determination

1. *U.S. population.* Using the conservative exposure assumptions described above and based on the completeness and the reliability of the toxicity data, BASF has estimated that aggregate exposure to BAS 510 F will

utilize 34.1% of the RfD for the U.S. population. For the highest exposed age-related subpopulation (children 1–6 years), the maximum aggregate exposure is predicted to be 77.4% of the reference dose. BASF concludes that there is a reasonable certainty that no harm will result from the aggregate exposure to residues of BAS 510 F, including anticipated dietary and drinking water exposures and non-occupational exposures.

2. Infants and children—i.

Developmental toxicity in the Rat. A developmental study was conducted via oral gavage in rats with dosages of 0, 100, 300 and 1,000 mg/kg bw/day with a maternal and developmental No-Adverse-Effect Level (NOAEL) of 1,000 mg/kg. No evidence of developmental toxicity was observed up to the highest dose tested.

ii. *Developmental toxicity in the rabbit.* A developmental study was conducted via oral gavage in rabbits with dosages of 0, 100, 300 and 1,000 mg/kg bw/day. The NOAEL for maternal toxicity was 100 mg/kg bw/day and was 1,000 mg/kg/day for developmental toxicity. As noted above in section B.3. (Reproductive and developmental toxicity), this NOAEL is based on fecal alterations and an abortion in a single dam at the next highest dose of 300 mg/kg/day. The dam which displayed the fecal alterations and abortion also displayed decreased body weight, body weight gain and food consumption, compared to the group mean, during gestation. These decreases occurred even prior to compound administration. These decreases in body weight, body weight gain, and food consumption, prior to compound administration, all indicate an animal in poor health and this poor state of health, rather than compound exposure, was likely the reason for the fecal alterations and abortion. No teratogenic effects were observed at any dose level.

iii. *Reproductive toxicity.* A two-generation reproduction study in rats

was conducted with dosages of 0, 12, 118, and 1,183 mg/kg bw/day. No impairment of reproductive function was noted at any dose. The parental and developmental NOAEL are both 12 mg/kg/day. Mild effects in both the parents and pups were noted at 118 mg/kg/day and consisted of an increased incidence of hepatic centrilobular hypertrophy in parents and, in the pups, slightly decreased body weight and body weight gain (7%) in F₂ generation only, and only in males. At 1,183 mg/kg/day paternal effects included decreased body weights and food consumption, increased liver weights and increased incidence of hepatic centrilobular hypertrophy and degeneration. Pup effects at this dose were an increase in pup mortality in the F₂ only and a decreased body weight in F₁ and F₂.

iv. *Reference dose.* In all reproductive studies, the NOAEL’s for developmental effects were either equal to or higher than those for the parents. Therefore, BAS 510 F shows no selective toxicity for the young. In addition, there were no direct neurotoxicity effects noted in either the acute or subchronic neurotoxicity studies.

Based on these results, no additional safety factors to protect children are warranted. Since the reproductive studies NOAEL’s are higher than the RfD calculated from the chronic rat study, BASF believes the Reference Dose of 0.05 mg/kg/day is also appropriate to measure safety for infants and children. Therefore, the chronic Population Adjusted Dose (cPAD) is also 0.05 mg/kg bw/day.

F. International Tolerances

A maximum residue level (MRL) has not been established for BAS 510 F in any crop by the Codex Alimentarius Commission.

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A. Residue Chemistry

1. *Plant metabolism.* Nature of the residue studies (OPPTS Harmonized