

maximum tolerated dose (MTD). Given the lack of structural activity relationship (SAR) and the lack of mutagenicity discussed in section B.2., it is BASF's opinion that dimethenamid-P should not be considered a biologically relevant carcinogen in rats and the assessment is made that the results of this carcinogenicity study do not indicate a carcinogenic potential of the test substance for humans.

iii. *Carcinogenicity - mice.* A carcinogenicity study using dimethenamid in mice fed dosages of 0, 3.8, 41, 205, and 431 (HDT) mg/kg/day (males) and 0, 4.1, 41, 200, and 411 (HDT) mg/kg/day (females) with a NOAEL of 41 mg/kg/day for male and female mice based on the following effects: (1) Decreased body weights and food consumption were observed in both males and female mice at the highest dose tested; (2) increased liver weights were observed for male and female mice at the highest dose tested at an interim sacrifice and increased weights for kidney and liver were observed for female mice at dose levels > 200 mg/kg/day at terminal sacrifice; (3) microscopic findings were observed in the liver and stomach for both male and female mice at the upper dose levels; (4) concerning the finding in the stomach, EPA has determined that this finding was attributed to irritation of the material and the finding was not toxicology significant; and (4) no increased incidence of neoplasms occurred at any dose levels tested in this study. EPA has concluded that this product is not carcinogenic under the conditions of this study.

Dimethenamid is considered not to be carcinogenic in mice by BASF. In the rat carcinogenicity study, a slight increase in liver tumors was observed in males, only, at the highest dose tested. The liver tumors observed in this study occurred at an incidence that was slightly beyond the historical control range for this tumor type, and occurred at the MTD. Dimethenamid shares no common mechanisms with other compounds in the chloroacetanilide class of compounds. It is BASF's opinion that dimethenamid and dimethenamid-P should not be considered biologically relevant carcinogens in rats and the assessment is made that the results of this carcinogenicity study do not indicate a carcinogenic potential of these substances for humans.

However, EPA has determined that dimethenamid is considered to be a Group C carcinogen - possible human carcinogen - based on the judgment of the EPA Carcinogenicity Peer Review Committee assessment. Also, the

Committee determined for risk assessment purposes, the RfD approach should be used to quantify human risk. BASF agrees with the Agency that the RfD approach for human risk assessment is valid.

5. *Endocrine disruption.* No specific tests have been performed with dimethenamid-P or dimethenamid to determine whether the chemical may have an effect in humans that is similar to an effect produced by naturally occurring estrogen or other endocrine effects. However, there are no significant findings in other relevant toxicity studies, *i.e.* teratology and multi-generation reproductive studies, that would suggest the dimethenamid produces endocrine related effects.

C. Aggregate Exposure

1. *Dietary exposure—i. Food.* BASF has reviewed the available toxicology database to determine the endpoints of concern. For dimethenamid and dimethenamid-P, BASF believes there is no concern regarding an acute dietary risk since the available data do not indicate any evidence of significant toxicity from a 1 day or single event exposure by the oral route.

For the purpose of assessing the potential chronic dietary exposure, BASF has estimated aggregate exposure based on theoretical maximum residue contribution (TMRC) from the tolerance of dimethenamid on sweet corn, sorghum, peanuts, and dry beans at 0.01 ppm for all uses stated, respectively. The TMRC is a "worse case" estimate of dietary exposure since it is assumed that 100% of all crops for which the tolerances are established are treated and that pesticide residues are always found at tolerance levels. EPA in a letter issued on October 13, 1995, for dimethenamid, determined the TMRC for the crops mentioned in section C.1. to be 0.076 and 0.341 microgram (ug)/kg/day for the general U.S. population and non-nursing infants (< 1), respectively. Dimethenamid treated crops using the TMRC values utilized 0.15% and 0.683% for the general U.S. population and non-nursing infants (< 1), respectively, of the RfD (0.05 mg/kg/day). These assessments are also valid for dimethenamid-P. BASF concurs with this assessment.

The addition of an onion tolerance at 0.01 ppm has a TMRC of 0.0011 ug/kg/day for the general population and a TMRC of 0.0004 ug/kg/day for non-nursing infants. Sugar beet tolerances at 0.01 ppm, add 0.0033 ug/kg/day to the TMRC for the general population and 0.0013 ug/kg/day to the TMRC for non-nursing infants. The addition of table beet tops, dry bulb garlic, horseradish,

and dry bulb shallot is negligible; table beet root tolerances at 0.01 ppm add 0.00022 ug/kg/day to the TMRC for the general population and 0.0019 ug/kg/day to the TMRC for non-nursing infants. The addition of potato tolerances at 0.01 ppm would contribute 0.011 ug/kg/day to the TMRC for the general population and 0.014 ug/kg/day to the TMRC for non-nursing infants. The addition of sweet potato tolerances at 0.01 ppm would contribute 0.00039 ug/kg/day to the TMRC for the general population and 0.0029 ug/kg/day to the TMRC for non-nursing infants. The total RfD utilization from all uses, both registered and proposed, is 0.18% for the general population, and 0.72% for non-nursing infants.

Therefore, based on the completeness and reliability of the toxicity data, and the exposure assessment discussed in section C.1., BASF concludes that there is a reasonable certainty that no harm will result from aggregate exposure to residues of dimethenamid and dimethenamid-P, including all anticipated dietary exposure.

ii. *Drinking water.* Other potential sources of exposure to dimethenamid for the general population are residues in drinking water and exposure from non-occupational sources. In a dimethenamid-P environmental-fate risk assessment dated December 1998, EPA calculated the following maximum concentrations for drinking water: Based on SCI-GROW model calculations, ground-water concentrations were expected to be < 1.0 parts per billion (ppb). Based on PRZM/EXAMS model calculations for surface water, the maximum yearly average (chronic) concentration was 5.4 ug/l from a Southeast corn scenario. Using these values, the drinking water level of comparison (DWLOC) and the aggregate RfD utilization are summarized in the table below.

| | U.S. population (% of RfD) | Non-nursing infants (% of RfD) |
|--|----------------------------|--------------------------------|
| Chronic dietary exposure | 0.18 | 0.72 |
| Remainder RfD available for water (%) (drinking water level of comparison) | 99.82 | 99.32 |