

"blended" by EPA's Health Effects Division (HED) SOP 99.6, mean field trial residue data were used. As allowed in EPA's draft guidance for submission of probabilistic human health exposure assessments one half limit of detection limit of detection (LOD) limit of quantitation (LOQ) values were used for all non-detected values (values below the sensitivity of the method).

ii. *Acute.* Bayer Corporation's acute Monte Carlo dietary exposure assessment estimated percent of the aPAD and corresponding MOE for the overall U.S. population (all seasons) and various subpopulations. In this analysis, the exposure for the total U.S. population was equal to 7.73% of the aPAD at the 99.9<sup>th</sup> percentile. The most highly exposed population subgroup, children (1 to 6 yrs), had an exposure equal to 16.42% of the aPAD at the 99.9<sup>th</sup> percentile. Therefore, the acute dietary exposure estimates are below EPA's level of concern (LOC) for the overall U.S. population as well as the various subpopulations.

iii. *Chronic.* The Bayer Corporation chronic dietary exposure estimated the percent of the cPAD for the overall U.S. population (all seasons) and various subpopulations. In this analysis, the exposure for the total U.S. population was equal to 1.4% of the cPAD. The most highly exposed population subgroup, children (1 to 6 yrs), had an exposure equal to 3.0% of the cPAD. Therefore, the chronic exposure estimates are below EPA's LOC for the overall U.S. population as well as the various subpopulations.

iv. *Drinking water.* EPA, as published in the **Federal Register** of April 10, 2001 (69 FR 18554) (FRL-6777-6), calculated acute and chronic drinking water levels of concern (DWLOC) and compared them with the estimated environmental concentrations (EECs) for surface water and ground water. Based on this comparison, they determined that acute exposure and chronic exposure would not be expected to exceed the aPAD and cPAD, respectively. It is not expected that the additional exposure from the minor crops pending in EPA's 2002 work plan would significantly change EPA's water assessment.

2. *Non-dietary exposure—i. Residential turf.* Bayer Corporation has conducted an exposure study to address the potential exposures of adults and children from contact with imidacloprid treated turf. The population considered to have the greatest potential exposure from contact with pesticide treated turf soon after pesticides are applied are young children. Margins of safety (MOS) of 7,587–41,546 for 10-year old children and 6,859–45,249 for 5-year old

children were estimated by comparing dermal exposure doses to the imidacloprid no-observable effect level of 1,000 mg/kg/day established in a 15-day dermal toxicity study in rabbits. The estimated safe residue levels of imidacloprid on treated turf for 10-year old children ranged from 5.6 - 38.2 grams/centimeters (g/cm<sup>2</sup>) and for 5-year old children from 5.1 - 33.5 g/cm<sup>2</sup>. This compares with the average imidacloprid transferable residue level of 0.080 g/cm<sup>2</sup> present immediately after the sprays have dried. The data indicate that children can safely contact imidacloprid-treated turf as soon after application as the spray has dried.

ii. *Termiticide.* Imidacloprid is registered as a termiticide. Due to the nature of the treatment for termites, exposure would be limited to that from inhalation and was evaluated by EPA and the Bayer Corporation. Data indicate that the MOS for the worst case exposures for adults and infants occupying a treated building who are exposed continuously (24 hours/day) are  $8.0 \times 10^7$  and  $2.4 \times 10^8$ , respectively - and exposure can thus be considered negligible.

iii. *Tobacco smoke.* Studies have been conducted to determine residues in tobacco and the resulting smoke following treatment. Residues of imidacloprid in cured tobacco following treatment were a maximum of 31 ppm (7 ppm in fresh leaves). When this tobacco was burned in a pyrolysis study only 2% of the initial residue was recovered in the resulting smoke (main stream plus side stream). This would result in an inhalation exposure to imidacloprid from smoking of approximately 0.0005 mg per cigarette. Using the measured subacute rat inhalation NOAEL of 5.5 milligrams/meters (mg/m<sup>3</sup>), it is apparent that exposure to imidacloprid from smoking (direct exposure and/or indirect exposure) would not be significant.

iv. *Pet treatment.* Human exposure from the use of imidacloprid to treat dogs and cats for fleas has been addressed by EPA. Bayer Corporation believes, that due to the fact that imidacloprid is not an inhalation or dermal toxicant and that while dermal absorption data are not available, imidacloprid is not considered to present a hazard via the dermal route.

#### D. Cumulative Effects

Imidacloprid is a chloronicotinyl insecticide. At this time, EPA has not made a determination that imidacloprid and other substances that may have a common mechanism of toxicity would have cumulative effects. Therefore, for these tolerance petitions, Bayer

Corporation assumes that imidacloprid does not have a common mechanism of toxicity with other substances and only the potential risks of imidacloprid in its aggregate exposure are considered.

#### E. Safety Determination

1. *U.S. population.* EPA has considered data from developmental toxicity studies in the rat and rabbit and a 2-generation reproduction study in the rat. These studies are discussed in the toxicological profile section of Unit II. of the **Federal Register** dated September 18, 1998 (63 FR 49837). The developmental toxicity data demonstrated no increased sensitivity of rats or rabbits to *in utero* exposure to imidacloprid. In addition, the multi-generation reproductive toxicity study did not identify any increased sensitivity of rats to *in utero* or postnatal exposure. Parental NOAELs were lower or equivalent to developmental or offspring NOAELs. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from maternal pesticide exposure during gestation. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability of mating animals and data on systemic toxicity.

FFDCA section 408 provides that EPA shall apply an additional ten-fold margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the data base unless EPA determines that a different margin of safety will be safe for infants and children. Margin of safety are incorporated into EPA risk assessments either directly through use of a MOE analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. EPA believes that reliable data support using the standard UF (usually 100 for combined interspecies and intraspecies variability) and not the additional ten-fold MOE/UF when EPA has a complete data base under existing guidelines and when the severity of the effect in infants or children or the potency or unusual toxic properties of a compound do not raise concerns regarding the adequacy of the standard MOE/SF.

Although developmental toxicity studies showed no increased sensitivity in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits, no increased sensitivity in pups as compared to adults was seen in the 2-generation reproduction toxicity study in rats, and the toxicology data base is complete as to core