

Children $(200 \mu\text{g/L} \times 10^{-3} \text{ mg}/\mu\text{g} \times 1 \text{ L/day}) / 10 \text{ kg} = 0.02 \text{ mg/kg/day}$

The degree of risk can be characterized by the magnitude of the margin of exposure (MOE), which is the ratio of the NOAEL from the animal toxicity study used to set the RfD to an estimated human exposure value ($\text{MOE} = \text{NOAEL}/\text{Human Exposure}$). Based on the NOAEL of 250 mg/kg b.w./day from the chronic dog study and children's exposure value (worst case) of 0.02 mg/kg b.w./day, a very high, favorable MOE of 12,500 times is derived. Thus, there is a reasonable expectation of no harm from the proposed and existing uses of imazapyr.

2. *Non-dietary exposure.* There is no available information quantifying non-dietary exposure to imazapyr. However, based on physical and chemical characteristics of the compound, the use patterns, and available information concerning its environmental fate, non-dietary exposure is expected to be negligible.

Previous registrations for imazapyr included non-crop sites. Labeled use sites for one group of imazapyr products include railroad, utility, pipeline, and highway rights-of-way, utility plant sites, petroleum tank farms, pumping installations, fence rows, storage areas, non-irrigation ditchbanks, under asphalt, under pond liners, wildlife management areas, forestry site preparation, and other non-crop areas. Imazapyr products for the above uses are clearly not intended for use in residential or recreational areas that have a high potential of exposure for the general population. The labels state that these imazapyr products are not for use on lawns, walks, driveways, tennis courts or similar areas.

Other imazapyr products are labeled as plant growth regulators for applications to limited care-low maintenance areas, such as roadsides, airports, fairgrounds, and golf course roughs, and to limited wear areas such as industrial, institutional, and cemetery grounds. These low rate uses entail minimal exposure potential for the general population. The product labeling does not allow use on turf that is being grown for sale or other commercial use, such as sod. There are imazapyr products marketed for residential use. These total vegetation control products are used for spot treatments or bare ground applications. These products are to be applied only where no plant growth is desired and are not to be used on lawns. Therefore, even for the limited residential uses, the potential for exposure is minimal.

For the aquatic use, a recreational swimmer risk assessment is not required

because no acute toxicological endpoints for oral, dermal, and inhalation routes of exposure were identified by EPA for imazapyr. Moreover, the dermal NOAEL for the 21-day rabbit toxicity study is the HDT (400 mg/kg b.w./day), indicating that imazapyr is non-toxic following repeated dermal exposure.

3. *Operator exposure.* Specifically, for potential short- and intermediate-term occupational exposure, professional contractors (representing worst-case for the proposed uses) would be mixing/loading/applying the end-use product for less than 90 days per year (and less than 30 consecutive days per year). Importantly, in its risk characterization of imazapyr for use in/on corn (1997), EPA found no toxicological endpoints indicating potential for adverse effects that were identified for short-term (1–7 days) and intermediate-term (7 days to several months) occupational exposure. In the 21-day dermal toxicity study, the NOAEL was determined to be 400 mg/kg b.w./day HDT. This was further supported by oral NOAELs of 250 mg/kg b.w./day HDT in the chronic dog study and 500 mg/kg b.w./day HDT (males) or 640 mg/kg b.w./day HDT (females) in the chronic rat study. Therefore, short- and intermediate-term risk assessments are not required.

D. Cumulative Effects

Imazapyr belongs to the imidazolinone class of compounds. Other compounds in this class are registered herbicides. However, the herbicidal activity of the imidazolinones is due to the inhibition of acetohydroxyacid synthase (AHAS), an enzyme only found in plants. AHAS is part of the biosynthetic pathway leading to the formation of branched chain amino acids. Animals lack AHAS and this biosynthetic pathway. This lack of AHAS contributes to the low toxicity of the imidazolinone compounds in animals. We are aware of no information to indicate or suggest that imazapyr has any toxic effects on mammals that would be cumulative with those of any other chemical.

E. Safety Determination

1. *U.S. population.* Based on the chronic RfD of 2.50 mg/kg b.w./day, the proposed application will utilize less than 0.1% of this value. Exposure estimates for the general U.S. population were only 0.000227 mg/kg b.w./day. Exposure estimates for children 1 to 6 years of age, the most highly exposed population group, were only 0.000575 mg/kg b.w./day or less than 0.1% of the RfD. EPA generally has no concern for exposure below 100% of

the RfD which represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. The complete and reliable toxicity data, indicating low potential mammalian toxicity, and the conservative chronic exposure assumptions support the conclusion that there is a "reasonable certainty of no harm" from aggregate exposure to imazapyr residues.

2. *Infants and children.* No developmental, reproductive or fetotoxic effects were noted at the highest doses of imazapyr tested. The only maternal effect in the rat teratology study was increased salivation in the highest dose group. The NOAEL used to calculate the RfD for the general U.S. population is 250 mg/kg b.w./day derived from the 1-year chronic toxicity study in dogs. That NOAEL is lower than the developmental NOAELs for the teratology studies in rabbits and rats (1.6 and 4 times, respectively), as well as lower than the NOAEL for the 2-generation reproduction study in male and female rats (3.2 - 3.9 times).

EPA has found the data base relative to prenatal and postnatal effects for children to be complete, valid and reliable. There were no effects observed in the offspring in the developmental studies in rats and rabbits. In the reproduction study, the lack of any pup effects observed at 10,000 ppm (the highest dose tested) in their growth and development from parturition through adulthood, suggests that there is no additional sensitivity for infants and children. Therefore, an additional safety (uncertainty) factor is not warranted and the RfD of 2.50 mg/kg b.w./day, which utilizes a 100-fold safety factor, is appropriate to assure a reasonable certainty of no harm to infants and children.

Therefore, the registrant believes that the results of the toxicology and metabolism studies support both the safety of imazapyr to humans based on the intended use as a herbicide for aquatic and grass uses and the granting of the requested tolerances.

F. International Tolerances

There are no Codex tolerances established for imazapyr.

[FR Doc. 03–20640 Filed 8–12–03; 8:45 am]

BILLING CODE 6560–50–S