

2. *Analytical method.* An adequate analytical method, gas chromatography/mass spectrometry (GC/MS) with selected ion monitoring, is available for enforcement purposes.

3. *Magnitude of residues.* Magnitude of the residue trials conducted on spring wheat, winter wheat, and barley showed no residues above the limit of quantification ((LOQ) = 0.02 ppm) on wheat grain, straw, hay, or processed commodities at the harvest timing prescribed by the label. Residues in forage ranged from <0.02 ppm to 0.03 ppm at 28 days posttreatment. Based on the results of animal metabolism studies, it is unlikely that significant residues would occur in secondary animal commodities from the use of tralkoxydim on wheat and barley. The nature of the residue in plants is adequately understood.

B. Toxicological Profile

1. *Acute toxicity.* EPA has established an acute reference dose (RfD) for tralkoxydim of 0.3 milligrams/kilogram/day (mg/kg/day). This RfD is based on the no observed adverse effect level (NOAEL) of 30 mg/kg/day established in the rat developmental study and using an uncertainty factor (UF) of 100 based on 10X for inter-species extrapolation and 10X for intra-species variation.

2. *Genotoxicity.* Tralkoxydim was negative for mutagenic/genotoxic effects in a gene mutation Ames Assay in bacteria, a forward gene mutation in mouse lymphoma cells in culture, chromosome damage/*in vitro* assay in human lymphocyte cells, deoxyribonucleic acid (DNA) damage repair *in vivo* assay in rat hepatocytes, and chromosome damage *in vivo* mouse micronuclei.

3. *Reproductive and developmental toxicity.* The developmental and reproductive toxicity data do not indicate increased susceptibility of rats or rabbits to *in utero* and/or postnatal exposure to tralkoxydim. A 3-generation rat reproduction study indicated a parental systemic NOAEL of 200 ppm, 20 mg/kg/day and a systemic lowest observed adverse effect level (LOAEL) of 1,000 ppm, 100 mg/kg/day based on reduced body weights and body weight gains in females. No reproductive toxicity was observed. A rat developmental study with a maternal NOAEL of 30 mg/kg/day and with a maternal LOAEL of 200 mg/kg/day based on maternal mortality, reduced body weights, and reduced food consumption and a developmental NOAEL of 30 mg/kg/day and a developmental LOAEL of 200 mg/kg/day based on reduced ossification of the centrum and hemicentrum, centrum

bipartite, misshapen centra and fused centra. A rabbit developmental study with a maternal NOAEL of 20 mg/kg/day and a maternal LOAEL of 100 mg/kg/day based on reduced food consumption and a developmental NOAEL of 20 mg/kg/day and a developmental LOAEL of 100 mg/kg/day based on abortions and increases in late resorptions.

4. *Subchronic toxicity.* Tralkoxydim is of low subchronic toxicity in 21-day dermal testing.

5. *Chronic toxicity.* EPA has established the RfD for tralkoxydim at 0.005 mg/kg/day. This RfD is based on NOAEL of 0.5 mg/kg/day in the chronic toxicity study in dogs with a 100-fold UF to account for interspecies extrapolation (10x) and intraspecies variability (10x). The Health Effects Division (HED) Cancer Assessment Review Committee (CARC) has classified tralkoxydim in accordance with the Agency's Proposed Guidelines for Carcinogen Risk Assessment (April 10, 1996), "likely to be human carcinogen." This classification is based on the following factors:

- Occurrence of benign Leydig cell tumors at all dose levels with the incidences at the high dose exceeding the concurrent and historical control range.
- Lack of an acceptable carcinogenicity study in a second species as required by OPPTS Harmonized Guidelines.
- The relevance of the testicular tumors to human exposure can not be discounted.

6. *Animal metabolism.* Based on the results of animal metabolism studies it is unlikely that significant residues would occur in secondary animal commodities from the use of tralkoxydim on wheat and barley.

7. *Metabolite toxicology.* The nature of the residue in barley, wheat, rotational crops, and livestock is adequately understood. The residues of concern for the tolerance expression are parent *per se*.

8. *Endocrine disruption.* There has been no evidence of endocrine disruption concerns with resulting from tralkoxydim use on wheat and barley.

C. Aggregate Exposure

1. *Dietary exposure.* The proposed tolerances in or on RACs: Barley grain, barley hay, wheat grain, and wheat hay at 0.02 ppm, and barley straw, wheat forage, and wheat straw at 0.05 ppm are the first to be established for tralkoxydim. There is no reasonable expectation of residues of tralkoxydim occurring in meat, milk, poultry, or eggs from its use on wheat and barley. Risk

assessments were conducted by EPA to assess dietary exposures from tralkoxydim as follows:

i. *Acute exposure and risk.* Acute dietary risk assessments are performed for a food-use pesticide if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a 1-day or single exposure. An acute dietary risk assessment was conducted for tralkoxydim based on the NOAEL of 30 milligram/kilogram/day (mg/kg/day) from the rat developmental study. The acute dietary analysis using the dietary exposure evaluation model (DEEM) computer program estimates that the distribution of single-day exposures utilizes 0.02% of acute RfD.

ii. *Chronic exposure and risk.* The RfD for tralkoxydim is 0.005 mg/kg/day. This value is based on the systemic NOAEL of 0.5 mg/kg/day in the dog chronic feeding study with a 100-fold safety factor to account for interspecies extrapolation (10x) and intraspecies variability (10x).

iii. *Food.* A DEEM chronic exposure analysis was conducted using tolerance levels for wheat and barley and assuming that 100% of the crop is treated to estimate dietary exposure for the general population and 22 subgroups. The chronic analysis showed that exposures from the tolerance level residues in or on wheat, and barley for children 1 to 6 years old (the subgroup with the highest exposure) would be 1.4% of the RfD. The exposure for the general U.S. population would be less than 1% of the RfD.

A lifetime dietary carcinogenicity exposure analysis was conducted for tralkoxydim using the proposed tolerances along with the assumption of 100% of the crop treated and a Q^* of 1.68×10^{-2} (mg/kg/day)⁻¹. A lifetime risk exposure analysis was also conducted using the DEEM computer analysis. The estimated cancer risk (5×10^{-7}) is less than the level that the Agency usually considers for negligible cancer risk estimates.

iv. *Drinking water.* Drinking water estimated concentrations (DWECS) for surface water (parent tralkoxydim) were calculated by EPA's pesticide root zone model (PRIZM) computer models to be an average of 9.1 parts per billion (ppb). the DWECS for ground water based on the computer model screening concentration in ground water (SCI-GROW2) were calculated to be an average of .016 ppb.

2. *Non-dietary exposure.* There are no non-food uses of tralkoxydim currently registered under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended. No non-dietary