

agricultural commodities at 0.02 parts per million (ppm) for kernels plus cob with husk removed, and 1.0 ppm for forage. Tolerances for residues of fluroxypyr MHE in or on field corn are being proposed in support of this registration as follows: Grain, 0.02 ppm; forage, 1.0 ppm; and stover, 0.5 ppm. Tolerances for residues of fluroxypyr MHE in or on sorghum as follows: Sorghum grain, 0.02 ppm; sorghum forage, 2.0 ppm; sorghum stover, 4.0 ppm. Tolerances for residues of fluroxypyr MHE in or on grasses as follows: Grass forage, 120 ppm; grass hay, 160 ppm; and grass silage, 100 ppm. Based on the above tolerances and an animal feeding study, increased tolerances are also proposed for fluroxypyr MHE and fluroxypyr, expressed as combined residues of total fluroxypyr, in or on the following animal commodities: Milk of cattle, goats, hogs, horses and sheep, 0.3 ppm; and kidney of cattle, goats, hogs, horses and sheep, 1.5 ppm. EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data support granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

1. *Plant metabolism.* Fluroxypyr is a systemic herbicide that is readily translocated and rapidly converts to the acid form following absorption. Fluroxypyr moves readily throughout the plant via the phloem (nutrient transporting) system and to a lesser extent through the xylem (water-transporting). Fluroxypyr is distributed throughout the entire plant, including the meristems and other developing plant parts.

2. *Analytical method.* There is a practical method (GC with MS detection) for measuring levels of fluroxypyr MHE in or on food with a limit of detection that allows monitoring of food with residues at or above the levels set for, the proposed tolerances. Fluroxypyr has been tested through the FDAs Multi-residue Methodology, Protocols C, D, and E. The results have been published in the FDA Pesticide Analytical Manual, Volume I.

3. *Magnitude of residues.* The metabolism of fluroxypyr MHE in plants and animals (goats and poultry) is adequately understood for the purposes of these tolerances. Magnitudes of residue studies were conducted for field corn, sweet corn, sorghum and grasses. A process products study was not

conducted in field corn since residues of fluroxypyr MHE were not detected in corn grain at 5X the application rate. In addition, processing of sorghum was not conducted since residue data for flour are not required at this time because sorghum flour is used exclusively in the U.S. as a component for drywall, and not as either a human food or a feedstuff. No residues of fluroxypyr are expected in root or leafy vegetable crops grown in rotation to fluroxypyr-treated field corn, sweet corn, sorghum, and grasses, after a 30-day plant-back interval at the maximum allowable label rate of 8 oz active ingredient/Acre. Field corn, sweet corn, sorghum and grasses grown in rotation may contain low levels of fluroxypyr residues; however, the tolerance values proposed for these crops will adequately assure compliance with the labeled use patterns.

B. Toxicological Profile

1. *Acute toxicity.* Fluroxypyr MHE has low acute toxicity. The rat oral LD₅₀ is >5,000 milligrams/kilogram (mg/kg), the rabbit dermal LD₅₀ is >2,000 mg/kg, and the rat inhalation LC₅₀ is >1.0 mg/L (1,000 mg/cubic meter). In addition, fluroxypyr MHE is not a skin sensitizer in guinea pigs, has no dermal irritation in rabbits, and shows mild ocular irritation in rabbits. The end use formulation of fluroxypyr MHE has a similar low acute toxicity profile.

2. *Genotoxicity.* Short-term assays for genotoxicity consisting of a bacterial reverse mutation assay (Ames test), an *in vitro* assay for cytogenetic damage using the Chinese hamster ovary cells, an *in vitro* chromosomal aberration assay using rat lymphocytes, and an *in vivo* cytogenetic assay in the mouse bone marrow (micronucleus test) have been conducted with fluroxypyr MHE. These studies show a lack of genotoxicity. In addition, short-term assays for genotoxicity consisting of an Ames metabolic activation test, possible induction of point mutations at the HGPRT-Locus of Chinese hamster ovary cells, *in vivo* and *in vitro* chromosomal aberrations in the Chinese hamster ovary cells, unscheduled DNA synthesis in human embryonic cells, and an assay in mouse lymphoma cells have been conducted with fluroxypyr. These studies also show a lack of genotoxicity.

3. *Reproductive and developmental toxicity.* Developmental studies in rats and rabbits were conducted with both fluroxypyr MHE and fluroxypyr. Studies with fluroxypyr MHE showed maternal and fetal no observed adverse effect levels (NOAELs) of 300 mg/kg/day (rat) and 500 mg/kg/day (rabbit). Studies with fluroxypyr showed NOAELs in the rat of 250 mg/kg/day for maternal effects

and 500 mg/kg/day for fetal effects and a NOAEL in the rabbit of 250 mg/kg/day for both maternal and fetal effects. These studies show that fluroxypyr and fluroxypyr MHE are not teratogenic nor will they interfere with *in utero* development. Two multi-generation reproduction studies were conducted with fluroxypyr in rats. The first in Wistar rats showed no effect on fertility or reproductive performance and had a NOAEL of 500 mg/kg/day (highest dose tested). The second study in Sprague-Dawley rats showed a parental NOAEL for systemic effects of 100 mg/kg/day in male rats and 500 mg/kg/day in female rats. The NOAEL for reproductive effects was 750 mg/kg/day for males and 1,000 mg/kg/day for females (highest dose tested). The NOAEL for neonatal effects was 500 mg/kg/day.

4. *Subchronic toxicity.* Fluroxypyr MHE showed a NOAEL of 1,000 mg/kg/day in a 90-day rat dietary study and a 21-day rabbit dermal study. Ninety-day feeding studies with fluroxypyr showed NOAELs of 80 mg/kg/day (Wistar rats), 700 mg/kg/day (Fischer 344 rats), 1,342 mg/kg/day (male mice), and 1,748 mg/kg/day (female mice). In a 4-week dietary, range finding study with fluroxypyr in dogs, the NOAEL found was >50 mg/kg/day.

5. *Chronic toxicity.* Based on chronic testing with fluroxypyr in the mouse, dog, and rat (two studies), a reference dose (RfD) of 0.8 mg/kg/day is proposed for fluroxypyr and fluroxypyr MHE. The RfD has incorporated a 100-fold safety factor to the NOAEL found in the rat chronic test. NOAELs found in the chronic dietary studies are as follows: 150 mg/kg/day (dog), 300 mg/kg/day (mouse), 80 mg/kg/day (Wistar rats), 100 mg/kg/day (male Fischer 344 rats), and 500 mg/kg/day (female Fischer 344 rats).

6. *Animal metabolism.* Both fluroxypyr and fluroxypyr MHE have been evaluated in rat metabolism studies. In summary, these studies show that fluroxypyr MHE is rapidly hydrolyzed and the fate of the hydrolysis products, fluroxypyr and 1-methylheptanol, are independent of whether they were given as the ester or the acid. Fluroxypyr, *per se*, was extensively absorbed and rapidly excreted principally unchanged in the urine; 1-methylheptanol also was rapidly absorbed and rapidly eliminated. Repeated administration of fluroxypyr MHE was not associated with accumulation in tissues. Also, the metabolism and pharmacokinetics of 1-methylheptanol are comparable to that of the methylheptyl portion of fluroxypyr MHE.

7. *Metabolite toxicology.* Administration of fluroxypyr, as the