

2-amino-4-(hydroxymethylphosphinyl)-, monoammonium salt) and its metabolites, 3-methylphosphinopropionic acid, and 2-acetamido-4-methylphosphinobutanoic acid expressed as 2-amino-4-(hydroxymethylphosphinyl)butanoic acid equivalents in or on the raw agricultural commodities derived from transgenic cotton and rice tolerant to glufosinate-ammonium: Rice, grain at 1.0 ppm; rice, straw at 2.0 ppm; rice, hull at 2.0 ppm; cotton, undelinted seed at 4.0 ppm; and cotton, gin byproducts at 15.0 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 supports granting of the petition. Additional data may be needed before EPA rules on the petition.

#### A. Residue Chemistry

1. *Plant metabolism.* Metabolism studies have been conducted on crops tolerant to glufosinate-ammonium using radiolabeled parent. As a result, the nature of residues found in cotton, rice, and other transgenic crops tolerant to glufosinate ammonium is well understood. The principal residue in raw agricultural commodities at harvest was 3-methylphosphinopropionic acid (Hoe 061517). Other relevant residues are *N*-acetyl-*L*-glufosinate (2-acetamido-4-methylphosphinobutanoic acid, Hoe 099730) and lesser amounts of the parent compound.

2. *Analytical method.* The enforcement analytical method utilizes gas chromatography for detecting and measuring levels of glufosinate-ammonium and metabolites with a general limit of quantification of 0.05 ppm. This method allows detection of residues at or above the proposed tolerances.

3. *Magnitude of residues.* Field residue trials were conducted across the major regions of rice and cotton production in the United States. The treatment regime was selected to represent the use pattern that is the most likely to result in the highest residues. When sampled at 70 days or more after the last application glufosinate-ammonium derived residues did not exceed 0.74 ppm in rice grain and 1.48 ppm in rice straw; whereas, in cotton seed and gin by products the highest mean residue level was 3.2 ppm and 10.58 ppm, respectively. No concentration of the residues occurred when rice whole grain was processed into polished grain and bran, whereas a concentration factor of approximately

2.3 was found for rice hulls. After ginning, the cotton seed was processed into meal, hulls, and refined oil. No concentration of the residues upon processing of the cotton seed was observed.

#### B. Toxicological Profile

1. *Acute toxicity.* Glufosinate-ammonium has been classified as toxicity category III for acute oral, dermal, and inhalation toxicity; and for eye irritation. Glufosinate-ammonium is not a dermal irritant (toxicity category IV) nor is it a dermal sensitizer. The oral LD<sub>50</sub> is 2,000 milligrams/kilogram (mg/kg) in male rats and 1,620 mg/kg in female rats.

2. *Genotoxicity.* Based on results of a complete genotoxicity data base, there is no evidence of mutagenic activity in a battery of studies, including: *Salmonella* spp., *E. coli*, *in vitro* mammalian cell gene mutation assays, mammalian cell chromosome aberration assays, *in vivo* mouse bone marrow micronucleus assays, and unscheduled DNA synthesis assays.

3. *Reproductive and developmental toxicity.* In a developmental toxicity study, groups of 20 pregnant female Wistar rats were administered glufosinate-ammonium by gavage at doses of 0, 0.5, 2.24, 10, 50, and 250 mg/kg/day from days 7 to 16 of pregnancy. The no observed adverse effect level (NOAEL) for maternal toxicity is 10 mg/kg/day; the lowest observed adverse effect level (LOAEL) is 50 mg/kg/day based on vaginal bleeding and hyperactivity in dams. In the fetus, the NOAEL is 50 mg/kg/day, based on dilated renal pelvis observations at the LOAEL of 250 mg/kg/day. In a developmental toxicity study, groups of 15 pregnant female Himalayan rabbits were administered glufosinate-ammonium by gavage at doses of 0, 2.0, 6.3, or 20.0 mg/kg/day from days 7 to 19 of pregnancy. In maternal animals, decreases in food consumption and body weight gain were observed at the 20 mg/kg/day dose level. The NOAEL for maternal toxicity was 6.3 mg/kg/day and that for developmental toxicity was 20 mg/kg/day.

In a multi-generation reproduction study, glufosinate-ammonium was administered to groups of 30 male and 30 female Wistar/Han rats in the diet at concentrations of 0, 40, 120, or 360 ppm. The LOAEL for systemic toxicity is 120 ppm based on increased kidney weights in both sexes and generations. The systemic toxicity NOAEL is 40 ppm. The LOAEL for reproductive/developmental toxicity is 360 ppm based on decreased numbers of viable

pups in all generations. The NOAEL is 120 ppm.

4. *Subchronic toxicity.* In a subchronic oral toxicity study, glufosinate-ammonium was administered to 10 NMRI mice/sex/ dose in the diet at levels of 0, 80, 320, or 1,280 ppm (equivalent to 0, 12, 48, or 192 milligrams/kilogram/day (mg/kg/day)) for 13 weeks. Significant ( $p < 0.05$ ) increases were observed in serum aspartate aminotransferase and in alkaline phosphatase in high-dose (192 mg/kg/day) males. Also observed were increases in absolute and relative liver weights in mid-(48 mg/kg/day) and high-dose males. The NOAEL is 12 mg/kg/day, the LOAEL is 48 mg/kg/day based on the changes in clinical biochemistry and liver weights.

5. *Chronic toxicity.* In a combined chronic toxicity/oncogenicity study, glufosinate-ammonium was administered to 50 Wistar rats/sex/dose in the diet for 130 weeks at dose levels of 0, 40, 140, or 500 ppm (mean compound intake in males was 0, 1.9, 6.8, and 24.4 mg/kg/day and for females was 0, 2.4, 8.2, and 28.7 mg/kg/day, respectively). A dose-related increase in mortality was noted in females at 140 and 500 ppm, whereas in males increased absolute and relative kidney weights were noted at 140 ppm and 500 ppm. The NOAEL was considered to be 40 ppm. No treatment-related oncogenic response was noted.

In an oncogenicity study, glufosinate-ammonium was administered to 50 NMRI mice/sex/dose in the diet at dose levels of 0, 80, 160 (males only) or 320 (females only) ppm for 104 weeks. The NOAEL for systemic toxicity is 80 ppm (10.82/16.19 mg/kg/day in males/females (M/F)), and the LOAEL is 160/320 ppm (22.60/63.96 mg/kg/day in M/F), based on increased mortality in males, increased glucose levels in males and females, and changes in glutathione levels in males. No increase in tumor incidence was found in any treatment group.

In a chronic feeding study, technical glufosinate-ammonium was fed to male and female beagle dogs for 12 months in the diet at levels of 2.0, 5.0, or 8.5 mg/kg/day. The NOAEL is 5.0 mg/kg/day based on clinical signs of toxicity, reduced weight gain and mortality 8.5 mg/kg/day.

In a rat oncogenicity study, glufosinate-ammonium was administered to Wistar rats (60/sex/group) for up to 24 months at 0, 1,000, 5,000, or 10,000 ppm (equivalent to 0, 45.4, 228.9, or 466.3 mg/kg/day in males and 0, 57.1, 281.5, or 579.3 mg/kg/day in females). The LOAEL for chronic toxicity is 5,000 ppm (equivalent to