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SUPPLEMENTARY INFORMATION: The Interregional Research Project No. 4 (IR-4), New Jersey Agricultural Experiment Station, P.O. Box 231, Rutgers University, New Brunswick, NJ 08903, has submitted pesticide petition (PP) 4E4404 to EPA on behalf of the Agricultural Experiment Station of Washington. This petition requests that the Administrator, pursuant to section 408(e) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(e), amend 40 CFR 180.364(d) by establishing tolerances for residues of glyphosate (*N*-(phosphonomethyl)glycine) resulting from the application of the isopropylamine salt of glyphosate, in or on the raw agricultural commodities peppermint and spearmint at 200 parts per million (ppm).

The scientific data submitted in the petition and other relevant material have been evaluated. The toxicological data considered in support of the proposed tolerances include:

1. Several acute toxicology studies placing technical-grade glyphosate in Toxicity Category III (acute oral and dermal).

2. A 1-year chronic feeding study in dogs fed glyphosate in gelatin capsules containing 0, 20, 100, or 500 milligrams (mg)/kilogram (kg)/day with a no-observed-effect level (NOEL) established at 500 mg/kg/day. There were no toxic effects observed under the conditions of the study.

3. A 26-month chronic feeding carcinogenicity study in rats fed diets containing 0, 30, 100, or 300 ppm glyphosate (equivalent to 0/0, 3/3, 10/11, 31/34 mg/kg/day for males/females) with a NOEL for systemic toxicity established at 300 ppm. There were no treatment related systemic effects observed under the conditions of the study. The following findings were observed, however, in the high-dose groups when compared to the concurrent controls: (1) increased incidence of thyroid C-cell carcinomas in females; and (2) increased incidence of interstitial cell (Leydig cell) testicular tumors in males. EPA concluded that these neoplasms were not treatment related, and glyphosate was not considered to be carcinogenic in this study because the incidence of thyroid carcinomas was not statistically significant and the incidence of testicular tumors was within the historical incidence. This study is not considered an acceptable carcinogenic study since the feeding levels were not high enough to assess the carcinogenicity of glyphosate.

4. A 2-year chronic feeding/carcinogenicity study in rats fed diets containing 0, 2,000, 8,000, or 20,000 ppm (equivalent to 0/0, 89/113, 362/457, or 940/1,183 mg/kg/day for males/females) with a NOEL established at 8,000 ppm. Treatment-related systemic effects, which were only observed in the high-dose group, included decreased body weight gains in females, increased incidence of cataracts and lens abnormalities, decreased urinary pH, increased absolute liver weight, and increased liver/brain weight ratio in males. The study also showed slightly increased incidence of (1) pancreatic islet cell adenomas in the low-dose and high-dose males; (2) hepatocellular (liver) adenomas in the low-dose and high-dose males; and (3) thyroid C-cells adenomas in the mid-dose and high-dose male and females. EPA concluded that these adenomas were not treatment related, and glyphosate was not considered to be carcinogenic in this study.

5. A carcinogenicity study in mice fed diets containing 0, 150, 750, or 4,500 mg/kg/day for 18 months with a systemic NOEL established at 750 mg/kg/day. The following findings were observed in the high-dose group: (1) decreased body weight gain in males and females; (2) increased incidence of hepatocellular hypertrophy, hepatocellular necrosis and interstitial nephritis in males; (3) increased incidence of proximal tubule epithelial basophilia and hypertrophy in females; and (4) slightly increased incidence of renal tubular adenomas in males. EPA concluded that the occurrence of the renal tubular adenomas in male mice was spontaneous rather than compound induced because the incidence of these in males was not statistically significant when compared with the concurrent controls. Glyphosate was not considered to be carcinogenic in this study.

6. A developmental toxicity study in rats given gavage doses of 0, 300, 1,000, or 3,500 mg/kg/day of glyphosate during days 6 through 19 of gestation with a NOEL for developmental toxicity established at 1,000 mg/kg/day. There was an increase in the number of litters and fetuses with unossified sternebrae and a decrease in the fetal body weight at the 3,500-mg/kg/day dose.

7. A developmental toxicity study in rabbits given gavage doses of 0, 75, 175, or 350 mg/kg/day of glyphosate during days 6 through 27 of gestation. Developmental toxicity was not observed at any dose tested. The NOEL for developmental toxicity was established at 175 mg/kg/day. Due to high maternal mortality (10 of 16 females rabbits died) at the 350-mg/kg/day dose level, too few liters were available to adequately assess developmental toxicity at the high dose.

8. A three-generation reproductive study in rats fed diets containing 0, 3, 10, or 30 mg/kg/day with a systemic and reproductive NOEL of 30 mg/kg/day and a developmental NOEL of 10 mg/kg/day. The only effect observed was an increased incidence of focal tubular dilation of the kidney (both unilateral and bilateral combined) in the high-dose male F3b pups.

9. A two-generation reproductive study in rats fed diets containing 0, 100, 500, or 1,500 mg/kg/day of glyphosate with systemic and developmental NOEL's of 500 mg/kg/day and a reproductive NOEL of 1,500 mg/kg/day. Treatment-related effects, which were observed only in the high-dose group, include soft stools in the F0 and F1 males and females, decreased food consumption and body weight gain of the F0 and F1 males and females; and decreased body weight gain of the F1a, F2a, and F2b male and female pups during the second and third week of lactation.

10. A battery of mutagenicity studies including: gene mutation assay (Ames Test and assay in mammalian cells), negative; structural chromosomal aberration assay (cytogenic in vivo), negative; and other genotoxicity assays (rec-assay using *Bacillus subtilis* and reverse mutation assay using *Escherichia coli*), negative.

11. Metabolism studies in rats show that glyphosate is excreted in the urine and feces as the parent compound. Aminomethylphosphonic acid was the only metabolite excreted. Less than 1.0 percent of the absorbed dose remained in the tissues and organs, primarily in the bone tissue.

The dietary risk assessment for glyphosate indicates that there is minimal risk from established tolerances and the proposed tolerances for peppermint and spearmint. A cancer risk assessment is not appropriate for glyphosate since the pesticide is assigned to ''Group E'' (no evidence of carcinogenicity) of EPA's cancer classification system. Dietary risk assessments for the pesticide were conducted using the Reference Dose (RfD) to assess chronic exposure.

The RfD is calculated at 2 mg/kg/ of body weight/day based on a NOEL of 175 mg/kg/day from the rabbit developmental toxicity study and an uncertainty factor of 100. The theoretical maximum residue