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TEMPLATE:

[UPL NA Inc.]

[Insert petition number]

EPA has received a pesticide petition ([insert petition number]) from [UPL NA Inc.], [630 Freedom Business Center, Suite 402, King of Prussia, PA 19406; EPA Company Number 70506] requesting, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180

1. by establishing a tolerance for residues of [Glufosinate-P-ammonium] in or on the following raw agricultural commodities: [Almond, hulls at 0.25 ppm; beet, sugar, molasses at 2.5 ppm; beet, sugar, roots at 0.45 ppm; bushberry subgroup 13b at 0.075 ppm; canola, meal at 0.55 ppm; canola, seed at 0.2 ppm; cattle, fat at 0.2 ppm; cattle, meat at 0.075 ppm; cattle, meat byproducts at 3 ppm; corn, field forage at 2 ppm; corn, field, grain at 0.1 ppm; corn, field, stover at 3 ppm; corn, sweet, forage at 0.75 ppm; corn, sweet, kernels plus cob with husks removed at 0.15 ppm; corn, sweet, stover at 3 ppm; cotton, gin byproducts at 15 ppm; cotton, undelinted seed at 7.5 ppm; egg at 0.075 ppm; citrus fruit (crop group 10-10) at 0.075 ppm; pome fruit (crop group 11-10) at 0.125 ppm; stone fruit (crop group 12-12) at 0.15 ppm; goat, fat at 0.2 ppm; goat, meat at 0.075 ppm; goat, meat byproducts at 3 ppm; grain aspirated fractions at 12.5 ppm; grape at 0.025 ppm; hog, fat at 0.2 ppm; hog, meat at 0.075 ppm; hog, meat byproducts at 3 ppm; horse, fat at 0.2 ppm; horse, meat at 0.075 ppm; horse, meat byproducts at 3 ppm; milk at 0.075 ppm; tree nut (crop group 14-12) at 0.25 ppm; olive at 0.25 ppm; potato at 0.4 ppm; potato, chips at 0.8 ppm; potato granules/flakes at 1 ppm; poultry, fat at 0.075 ppm; poultry, meat at 0.075 ppm; poultry, meat byproducts at 0.3 ppm; sheep, fat at 0.2 ppm; sheep, meat at 0.075 ppm; sheep, meat byproducts at 3 ppm; soybean at 1 ppm; and soybean, hulls at 5 ppm].

Additionally inadvertent tolerances are proposed for the following commodities: [Barley, hay at 0.2 ppm; barley, straw at 0.2 ppm; buckwheat, fodder at 0.2 ppm; buckwheat, forage at 0.2 ppm; oat, forage at 0.2 ppm; oat, hay at 0.2 ppm; oat, straw at 0.2 ppm; rye, forage at 0.2 ppm; rye, straw at 0.2 ppm; teosinte at 0.2 ppm; triticale at 0.2 ppm; wheat, forage at 0.2 ppm; wheat, hay at 0.2 ppm; and wheat, straw at 0.2 ppm]. EPA has determined that the petition contains data or information regarding the elements set forth in section 408 (d)(2) of FDDCA; 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.* There is a robust residue chemistry database of studies for the racemic mixture allowing for an understanding of what residues for parent and metabolites might be present in crops, processed commodities, and meat, milk, poultry, and eggs from livestock animals consuming glufosinate treated feedstuffs. Studies conducted with crops using glufosinate, glufosinate-P, and glufosinate-M, identified as the L- and D- isomers, respectively (Ruhland, 2002 and 2004) showed that there was no difference in the metabolism pathways observed for the racemic and P-isomer and M-isomer, concluding that no new metabolites and thus residues of concern are expected when applying enriched glufosinate-P-ammonium.

2. *Analytical method.* Analytical methods for plant, soil, and water matrices have been developed, validated, and independently validated. These studies are summarized in the Environmental Fate and Residue Chemistry Volumes (MRIDs 51929415 and 51929432).

3. *Magnitude of residues*. Residue trials in all proposed crops were conducted in the appropriate regions across the United States in accordance with EPA guidance for crop field trials under OPPTS 860.1500.

B. Toxicological Profile

1. *Acute toxicity.* Glufosinate-p-ammonium has been classified as USEPA toxicity category III for acute oral, dermal, and inhalation toxicity; and category IV for eye irritation. Glufosinate-ammonium is not a dermal irritant (toxicity category IV) nor is it a dermal sensitizer. The oral LD50 is 937 mg/kg in female rats**.**

2. *Genotoxicity.* Based on results of a complete genotoxicity database for racemic glufosinate, there is no evidence of mutagenic activity in a battery of studies, including: an Ames assay, an *in vitro* mammalian cell gene mutation assays, a bacterial DNA damage and repair assay, an *in vivo* mouse bone marrow micronucleus assays, and an unscheduled DNA synthesis assays. Ames and *in vivo* micronucleus studies for Glufosinate-p-ammonium were conducted and the overall *in vitro* and *in vivo* datasets support the conclusion that glufosinate-P ammonium is not indicated for genotoxicity. The genotoxicity dataset is considered complete and acceptable to support the registration of glufosinate-P ammonium.

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 NOAEL for maternal toxicity is 10 mg/kg/day; the 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**.**

A prenatal developmental study in Chinchilla rabbits was conducted with enriched glufosinate-P ammonium at doses of 0, 1.25, 2.50, and 5.00 mg/kg. Observed decreases in body weight gains and food consumption, neurotoxic signs, and abortions were observed at the LOAEL of 2.5 mg/kg/day with a NOAEL of 1.25 mg/kg for both maternal and development effects. No teratogenic effects were observed for glufosinate-P ammonium.

In a multi-generation reproduction study, the NOAEL for parental toxicity was 360 ppm (equal to 18 mg/kg/day), the highest dose tested, which corresponds to a dose level of 180 ppm (equal to 9 mg/kg/day) glufosinate-P ammonium. The racemic glufosinate NOAEL for offspring toxicity was 120 ppm (equal to 6.0 mg/kg/day) based on a decrease in viable pups observed in all litters of both generations at 360 ppm (equal to 18 mg/kg/day), which corresponds to a dose level of 60 ppm (equal to 3.0 mg/kg/day). The glufosinate-P ammonium NOAEL for reproductive effects was 360 ppm (equal to 18 mg/kg/day) as there were no effects on fertility at any dose level, which corresponds to a dose level of 180 ppm (equal to 9 mg/kg/day).

In a developmental neurotoxicity study, racemic glufosinate was administered in the diet to 25 mated female Crl:CD®(SD)IGS BR rats/dose at nominal concentrations of 0 (control), 200, 1000, or 4500 ppm from gestation day (GD) 6 through lactation day (LD) 21, which corresponds to 0 (control), 100, 500, or 2250 ppm glufosinate-P ammonium. Average doses to the animals were 0, 14, 69, or 292 mg/kg/day during gestation and 0, 36, 176, or 746 mg/kg/day during lactation for the 0, 200, 1000, or 4500 ppm groups, respectively, which correspond The offspring LOAEL is 1000 ppm (69 mg/kg/day) based on brain morphometric changes (decrease in the mean length of the ventral limb of the dentate hilus), increased motor activity, and decreased body weight (US EPA, 2021). The offspring NOAEL is 200 ppm (14 mg/kg/day), which corresponds to a glufosinate-P-ammonium NOAEL of 7 mg/kg/day.

4. *Subchronic toxicity.* In a sub-chronic 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 mg/kg bw/day) for 13 weeks. These dose levels are equivalent to 0 (control), 40, 160, or 640 ppm (equal to 0, 6, 24, or 96 mg/kg/day) glufosinate-P ammonium. The NOAEL for males and females is the highest dose tested of 192 mg/kg/day racemic glufosinate, which is equivalent to 96 mg/kg/day (glufosinate-P ammonium) as there was no indication of adverse effects, with the observed increased in male liver weights and associated clinical chemistry effects being adaptive effects with no associate pathology.

5. *Chronic toxicity.* In the racemic glufosinate toxicological dataset submitted to and accepted by US EPA, there is an oral combined chronic toxicity and carcinogenicity study in rats (24.4 mg/kg racemic and 12.2 mg/kg glufosinate-p-ammonium), an oral carcinogenicity study in rats (45.4 mg/kg racemic and 22.7 mg/kg glufosinate-p-ammonium), an oral carcinogenicity study in mice (10.82 mg/kg racemic and 5.4 mg/kg glufosinate-p-ammonium), and an oral chronic toxicity study in dogs (5.0 mg/kg racemic and 2.5 mg/kg glufosinate-p-ammonium). No treatment-related oncogenic outcomes were observed in any study and, therefore, it can be concluded that glufosinate-P ammonium is not carcinogenic.

6. Animal metabolism. Groups of Wistar rats (5/sex or 2/sex) received a single dose (500 mg/kg) of ^{14}C-HOE 039866 (racemic glufosinate) by gavage. Animals were sacrificed at various times (2, 6, 24, and 96 hrs) after dosing. The majority of the radioactivity was eliminated during the first 24 to 48 hrs after dosing. The parent compound, racemic glufosinate, accounted for the majority of the radioactivity eliminated in the excreta of both males (~80% of the dose) and females (88% of the dose). The metabolite, glufosinate propanoic acid, was consistently found in both urine (0.22-1.20% of the dose) and feces (0.44-1.36% of the dose) of both sexes. N-acetylglufosinate was found in feces (0.28-1.72% of the dose) of both male and female rats and barely above or at the level of the detection in the urine of both sexes (0.02-0.04% of the dose). 2-hydroxy-4-methylphosphinico-butanoic acid was mainly found in the feces of both male and females (~0.2-0.28% of the dose). Very little if any of the administered racemic glufosinate was sequestered in the tissues.

A second group of Wistar rats (5/sex) were orally administered a single nominal dose (30 mg/kg) of 14C-HOE 039866 (racemic glufosinate). Rapid elimination during the first 24 hrs for both males and females was observed. The major route of excretion was via feces (88% and 84% of the administered radioactivity for males and females, respectively). Within seven days of post dosing, greater than 94% of the dose was eliminated. Kinetics analysis indicated that the process of excretion was a two-phase process. The tissue radioactivity level for kidneys, liver, and gonads was just above the background level.

A third group of Wistar rats (6/sex) were orally administered (gavage) unlabeled HOE 039866 (racemic glufosinate) at 2.0 mg/kg/day for 14 days and ^{14}C-HOE 039866 at the 15th day at a nominal dose of 2 mg/kg. The majority of the radioactivity was excreted within 24 hrs after the last dose. The major route of elimination was via feces. There was also a two-phased elimination process. More radioactivity was found in the tissues of animals dosed repeatedly than that of animals receiving a single dose.

7. *Metabolite toxicology*. The data package supports the conclusion that all metabolites have lower toxicity than glufosinate-p-ammonium.

8. *Endocrine disruption*. No evidence of estrogenic or other endocrine effects have been noted in any of the toxicology studies that have been conducted with this product, and there is no reason to suspect that any such effects would be likely.

C. Aggregate Exposure

1. Dietary exposure. [An acute dietary assessment was conducted to estimate exposure to potential glufosinate-P-ammonium residues on all proposed crops. The acute dietary assessment was conducted using EPA's software: DEEM-FCID v.4.02. The acute dietary exposure estimate for females 13-49 years from potential residues of glufosinate-P-ammonium was equivalent to 58.10 % of the aPAD (0.0125 mg/kg/day). Only females 13-49 years were assessed since an endpoint attributable to a single exposure was not determined from the toxicity studies all other population groups, including the developmental toxicity and developmental neurotoxicity studies. This assessment was very conservative as it was based on tolerance residue values and 100% crop treated.

A chronic dietary assessment was conducted to estimate exposure to potential glufosinate-P-ammonium residues on all proposed crops. The chronic dietary assessment was conducted using EPA's software: DEEM-FCID v.4.02. The chronic dietary exposure estimate for the U.S. population from potential residues of glufosinate-P-ammonium was equivalent to 17.3% of the cPAD (0.0125 mg/kg/day). The subpopulation with the highest dietary exposure was children 1-2 with exposure equivalent to 69.6% of the cPAD (0.0125 mg/kg/day). This assessment was very conservative as it was based on tolerance residue values and 100% crop treated.]

i. Food. [The tolerances used in the risk assessment described above were determined based on data submitted in support of the registration of the racemic mixture and are found at 40 CFR 180.473 (a,d). Please note that applying the enriched glufosinate-P-ammonium at a 50% reduced application rate has been shown by UPL to be of comparable efficacy to the racemic mixture and therefore a 50% reduction in residues was assumed in the assessments presented here.]

ii. Drinking water. [The estimated drinking water concentrations used in the dietary risk assessment were obtained from EPA's most recent estimated drinking water concentration (EDWC) for racemic glufosinate and incorporated directly into this dietary assessment (EPA, 2022; DP Barcode: D461847 and D461848). The acute and chronic EDWCs (201 ppb and 24.4 ppb, respectively) were adjusted by a factor of 50% to account for the lower use rates for glufosinate-P-ammonium. Water residues were incorporated in the DEEM-FCID residue file for food categories "water, direct, all sources" and "water, indirect, all sources."]

2. Non-dietary exposure. [Non-crop uses for glufosinate-P-ammonium include applications to dormant bermudagrass, ornamentals, Christmas trees, and uncropped farmstead areas. MOEs for all residential scenarios exceeded the level of concern (LOC) of 100. Therefore, the reasonable certainty of no harm standard has been met for the proposed uses.]

D. Cumulative Effects

[Cumulative Exposure to Substances with a Common Mechanism of Toxicity: Section 408(b)(2)(D)(v) requires that, when considering whether to establish, modify, or revoke a

tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity".

EPA consideration of a common mechanism of toxicity is not appropriate at this time since EPA does not have information to indicate that toxic effects produced by glufosinate-P-ammonium would be cumulative with those of any other chemical compounds; thus only the potential risks of glufosinate-P-ammonium are considered in this exposure assessment.]

E. Safety Determination

1. U.S. population. [The acute dietary exposure estimate for females 13-49 years from potential residues of glufosinate-P-ammonium was equivalent to 58.10 % of the aPAD (0.0125 mg/kg/day). Only females 13-49 years were assessed since an endpoint attributable to a single exposure was not determined from the toxicity studies all other population groups, including the developmental toxicity and developmental neurotoxicity studies. The chronic dietary exposure estimate for the U.S. population from potential residues of glufosinate-P-ammonium was equivalent to 17.3% of the cPAD (0.0125 mg/kg/day). Therefore, the reasonable certainty of no harm standard has been met for the proposed uses.]

2. Infants and children. [The subpopulation with the highest chronic dietary exposure was children 1-2 with exposure equivalent to 69.6% of the cPAD (0.0125 mg/kg/day). Therefore, the reasonable certainty of no harm standard has been met for the proposed uses.]

F. International Tolerances

There are no international tolerances for glufosinate-p-ammonium as this is a new active ingredient.