

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES



MEMORANDUM

Date: 20-June-2002

Subject: Glufosinate Ammonium (PC Code 128850). Section 3 Registrations for Transgenic Cotton (ID# - 0F06140), Transgenic Rice (ID# - 0F06210), and Bushberry (ID# - 2E06404). **Summary of Analytical Chemistry and Residue Data.** DB Barcodes: D271110, D271223, D282757, and D283373. Case Numbers: 292945, 293386, and 294699. Submission: S589377, S596735, and S609042. 40 CFR 180.473. MRIDs 45089302, 45089303, 45204404, 45204405, 45204407, 45204408, 45580201,

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Registration Division (7505C)

Aventis requested a Section 3 registration for application of glufosinate ammonium to transgenic rice, transgenic cotton, and cotton and proposed the establishment of the following permanent tolerances for the combined residues of glufosinate ammonium (butanoic acid, 2-amino-4-(hydroxymethylphosphinyl)-, monoammonium salt), 2-acetamido-4-methylphosphinico-butanoic acid, and 3-methylphosphinico-propionic acid expressed as glufosinate ammonium free acid equivalents (see attachment 1 for structures):

rice, grain	1.0 ppm
rice, straw	1.6 ppm
cotton, undelinted seed	3.5 ppm
cotton, gin byproducts	12 ppm

The Interregional Research Project Number 4 (IR-4) requested a Section 3 registration for application of glufosinate ammonium to blueberry and establishment of the following permanent tolerances for the combined residues of glufosinate ammonium (butanoic acid, 2-amino-4-(hydroxymethylphosphinyl)-, monoammonium salt) and 3-methylphosphinico-propionic acid:

·bushberry subgroup	0.10 ppm
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·the initial Section F proposed a tolerance in/on blueberry; via personnel communication with Hoyt Jamerson (RD), HED was informed the petitioner revised their proposal to include the entire bushberry crop sub-group

Recommendations

Section 3 registrations were requested by Aventis (transgenic rice and transgenic and nontransgenic cotton) and IR-4 (blueberry). A separate recommendation is written for each. A human health risk assessment will be prepared as a separate document.

Transgenic Rice and Transgenic and Nontransgenic Cotton: Provided the petitioner submits a revised Section F and a revised Section B, the residue chemistry database is sufficient for an unconditional registration and establishment of the following permanent tolerances for the combined residues of glufosinate ammonium (butanoic acid, 2-amino-4-(hydroxymethylphosphinyl) -, monoammonium salt), 2-acetamido-4-methylphosphinico-butanoic acid, and 3-methylphosphinico-propionic acid (all expressed as 2-amino-4-(hydroxymethylphosphinyl) butanoic acid):

rice, grain	1.0 ppm
rice, straw	2.0 ppm
rice, hull	2.0 ppm
cotton, undelinted seed	4.0 ppm
cotton, gin byproducts	15 ppm
egg	0.15 ppm
poultry, meat byproducts	0.60 ppm
poultry, meat	0.15 ppm
poultry, fat	0.15 ppm
milk	0.15 ppm
meat byproducts (cattle, goat, hog, horse, sheep)	6.0 ppm
meat (cattle, goat, hog, horse, sheep)	0.15 ppm
fat (cattle, goat, hog, horse, sheep)	0.40 ppm

Blueberry: Provided the petitioner submits a revised Section F, the residue chemistry database is sufficient for a conditional registration and establishment of the following permanent tolerances for the combined residues of glufosinate ammonium, 2-acetamido-4-methylphosphinico-butanoic acid, and 3-methylphosphinico-propionic acid (all expressed as 2-amino-4-(hydroxymethylphosphinyl) butanoic acid):

bushberry crop subgroup (13B)	0.15 ppm
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The residue chemistry database will be sufficient for unconditional registration provided the petitioner submits a blueberry field trial study conducted in Region 12 (n=1; residue decline data should be included).

Summary of Residue Chemistry Deficiencies

- revised Section B (see 860.1200 Directions for Use; 860.1400 Water, Fish, and Irrigated Crops; and 860.1850/860.1900 Confined/Field Accumulation in Rotational Crops)
- revised Section F (see 860.1500 Crop Field Trials; 860.1520 Processed Food and Feed; and 860.1480 Meat, Milk, Poultry, and Eggs)
- blueberry field trial (see 860.1500 Crop Field Trials)

Background

Technical glufosinate ammonium is a racemic mixture of the D and L enantiomers; only the L enantiomer is herbicidally active. The compound is a non-selective herbicide and acts as an inhibitor of glutamine synthetase which leads to poisoning of the plant by ammonia. Glufosinate ammonium is currently registered for use on both transgenic and nontransgenic crops. The transgenic plants currently registered (canola, sugar beet, corn, soybean) and the transgenic plants requested for registration (rice and cotton) have been engineered to express phosphiothrion-acetyl-transferase (PAT) which enables the plant to metabolize glufosinate ammonium into N-acetyl-glufosinate.

Current registrations include broadcast application to apple, grape, banana, potato (vine desiccant), and tree nut orchards with tolerances for the combined residues of glufosinate ammonium and 3-methylphosphonic propionic acid (both expressed as glufosinate free acid equivalents) ranging from 0.05 - 0.80 ppm (40 CFR 180.473). Glufosinate ammonium is also registered for application to the transgenic varieties of field corn, canola, sugar beet, and soybean with tolerances for the combined residues of glufosinate ammonium, 2-acetamido-4-methylphosphinico butanoic acid, and 3-methylphosphonic propionic acid (all expressed as glufosinate free acid equivalents) ranging from 0.2 - 25.0 ppm. Tolerances are also established for the combined residues of glufosinate ammonium and 3-methylphosphonic propionic acid (both expressed as glufosinate free acid equivalents) as a result of secondary residues in milk, eggs, and the meat, fat and meat byproducts of ruminants and poultry ranging from 0.02 ppm - 0.10 ppm.

The following terms may be used interchangeably (see attachment 1 for structures):

- HOE 039866 = butanoic acid, 2-amino-4-(hydroxymethylphosphinyl)-, monoammonium salt; represents both the D and L enantiomers
- HOE 099730 = N-acetyl-glufosinate = 2-acetamido-4-methylphosphinico butanoic acid; petitioner indicated that HOE 099730 represents only the L-enantiomer; the analytical method used in the magnitude of the residue, processing, feeding, and metabolism studies did not distinguish between the D and L enantiomers
- HOE 061517 = 3-methylphosphonic propionic acid
- glufosinate free acid = 2-amino-4-(hydroxymethylphosphinyl) butanoic acid

860.1200 Directions for Use

The petitioners have proposed application of Liberty® Herbicide (18.19% glufosinate ammonium; soluble concentrate; EPA Reg. No. 264-660) to cotton, transgenic cotton, and transgenic rice and Rely® Herbicide (11.33% glufosinate ammonium; soluble concentrate; EPA Reg. No. 264-652) to bushberries. The Liberty® label indicates a 120-day plant back interval (PBI) for all crops except wheat, barley, buckwheat, millet, oats, rye, sorghum, and triticale where a 70-day PBI is indicated. Both labels prohibit application through irrigation equipment. The Rely® label also prohibits aerial application. The following are summaries of the proposed application scenarios.

Transgenic-Rice: Glufosinate ammonium may be applied as a broadcast spray to transgenic rice from the 1-leaf stage through the mid-tillering stage of development at 0.37-0.44 lbs ai/acre. A maximum of 0.89 lbs ai/acre can be applied per season. Rice is not to be harvested until 70 days after the last application. Surfactant and crop oils are not to be added to the spray solution. A silicon-based anti-foam agent may be added to the spray solution (the formulated product contains an antifoaming agent). Glufosinate ammonium may be applied prior to or after the establishment of a permanent flood. If applied post-flood, the water level should be lowered so that 75% of the foliage is exposed. A minimum spray volume of 10 gallons/acre is indicated for both ground and aerial applications. The label indicates that rice grown for seed may be treated.

The label should include a statement prohibiting the use of rice paddy water for irrigation purposes, as a water source for livestock, and for raising crayfish. **A revised Section B is requested.**

Transgenic-Cotton: Glufosinate ammonium may be applied from planting through the early bloom stage. A maximum of two broadcast over the top applications are permitted at 0.26-0.52 lbs ai/acre (1.04 lbs ai/acre as a broadcast spray). A third application can be made with the spray directed to the lower third of the plant at 0.52 lbs ai/acre. The season maximum application rate is 1.57 lbs ai/acre. A retreatment interval (RTI) of 14 days is specified. Cotton is not to be harvested until 70 days after the last application. A minimum spray volume of 15 gallons/acre and 10 gallons/acre is indicated for ground and aerial applications, respectively. An antifoaming agent and ammonium sulfate may be added to the spray solution (the formulated product contains an antifoaming agent). The petitioner should amend the label indicating that following treatment of cotton, the field may only be rotated to a registered crop (see 860.1850 and 860.1900 Confined/Field Accumulation in Rotational Crops section). **A revised Section B is requested.**

Cotton: Glufosinate ammonium may be applied from planting through the early bloom stage using a hooded sprayer. A maximum of three applications are permitted at 0.26-0.52 lbs ai/acre (season maximum application rate of 1.57 lbs ai/acre). RTI of 14 days is specified. Cotton is not to be harvested until 70 days after the last application. A minimum spray volume of 15 gallons/acre and 10 gallons/acre is indicated for ground and aerial applications, respectively. An antifoaming agent and ammonium sulfate may be added to the spray solution (the formulated product contains an antifoaming agent). The label adequately explains the proposed application scenario for cotton.

Bushberry: Glufosinate ammonium is to be applied as a directed spray (broadcast, banded, or spot treatment) to undesirable vegetation in blueberry fields at up to 1.5 lbs ai/acre. Two applications are permitted per season with a RTI of 28 days (maximum of 3.0 lbs ai/acre/year). Bushberries are not to be harvested until 14 days after the last application. A minimum spray volume of 20 gallons/acre is indicated. A nonionic antifoaming agent may be added to the spray solution (the formulated product contains an antifoaming agent). Cover crops treated with glufosinate ammonium may not be fed to livestock. The label adequately explains the proposed bushberry application scenario.

860.1300 Nature of the Residue - Plants

HED has previously reviewed metabolism studies conducted with nontransgenic (corn, soybean, apple, and lettuce; 8F3607, J. Garbus, 14-Oct-1988 & 8-Aug-1990) and transgenic (corn, soybean, sugar beet, canola, and rice; D227386, M. Rodriguez, 7-Mar-1996; D257629, T. Bloem, 9-Jul-1999; 45204405.der.wpd) crops. The transgenic corn, soybean, sugar beet, canola, and rice investigated in the metabolism studies were engineered to express PAT which acetylates glufosinate (herbicidally active) to form N-acetyl-glufosinate (not herbicidally active).

HOE 061517 was the only metabolite identified in the nontransgenic studies (2-40% total radioactive residue (TRR); only soybean leaf, corn stover, and apples were analyzed). The petitioner demonstrated that 40% of the TRR in nontransgenic corn stover was incorporated into protein, starch, cellulose, and lignin. Glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 were the major residues identified in the transgenic crops (40-98% of the TRR). The petitioner demonstrated that for transgenic sugar beet leaves, surface residues are composed of a nearly equal mixture of the D and L enantiomers of glufosinate ammonium while interior residues are composed of almost exclusively D enantiomer of glufosinate ammonium. This indicates that only the L enantiomer of glufosinate ammonium was acetylated to form N-acetyl-glufosinate.

Based on the metabolism and magnitude of the residue studies, the Metabolism Assessment Review Committee (MARC) concluded that the residues of concern in the crops studied, for tolerance expression and risk assessment purposes, are glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 (D282757, T. Bloem, 9-May-2002). HED concludes that the results from the currently available metabolism studies may be translated to blueberry, cotton, transgenic cotton, and transgenic rice.

860.1300 Nature of the Residue - Livestock

HED has previously reviewed lactating goat and laying hen metabolism studies (8F3607, J. Garbus, 14-Oct-1988 & 8-Aug-1990; D211531, M. Rodriguez, 7-Mar-1996). Since more extensive residue identification was performed for the studies reviewed in D211531, only the metabolism studies summarized in D211531 are discussed. The maximum theoretical dietary burdens (MTDB) are as follows: poultry - 3.33 ppm; beef cattle - 15.38 ppm; dairy cattle - 15.22 ppm; and hogs - 8.89 ppm (see 860.1480 Meat, Milk, Poultry, and Eggs)

Lactating goat and laying hen metabolism were dosed with [3,4-¹⁴C]-HOE-039866 at 6.5x and 7.4x the MTDB for ruminants and poultry, respectively. TRRs in muscle and fat from both studies were <0.01 ppm and were not further analyzed. Kidney, liver, and milk from the goat study and egg and liver from the hen study were analyzed with 36-90% of the TRR identified as glufosinate ammonium and HOE 064619. N-acetyl-glufosinate was identified as a minor metabolite in both the goat and hen studies (≤5% TRR).

Since the majority of the livestock dietary burden originates from transgenic crops, N-acetyl-glufosinate will be the primary residue in/on treated feed commodities. N-acetyl-glufosinate was found as a minor metabolite in the [3,4-¹⁴C]-HOE-039866 livestock metabolism studies indicating that this compound is part of the glufosinate ammonium metabolic pathway for livestock. Based on the metabolism and feeding studies, the MARC determined that the residues of concern in livestock, for tolerance expression and risk assessment purposes, are glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 (D282757, T. Bloem, 9-May-2002).

860.1340 Residue Analytical Methods

Plants: Two analytical methods have been validated by the Analytical Chemistry Branch (ACB) for enforcement of the currently established tolerances: **(1)** nontransgenic - method HRAV-5A was validated by ACB for the determination of glufosinate ammonium and HOE 061517 in/on apple, grape, almond, soybean seed, corn grain, and corn forage (PP # 8F3607, J. Garbus, 14-Sep-1989) and **(2)** transgenic - method BK/01/99 was validated by ACB for determination of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 in/on canola seed and sugar beet root (D258420, T. Bloem, 19-Aug-2000). Both methods involve extraction with water, anion exchange chromatography, derivatization with trimethylorthoacetate, silica gel column clean-up, and quantification via gas chromatography with flame photometric detection (residues expressed as glufosinate free acid equivalents). Method BK/01/99 includes a cation ion exchange column prior to derivatization which fractionates glufosinate ammonium and N-acetyl-glufosinate and allows for speciation of these compounds (both compounds are derivitized to the same compound). This step can be eliminated if separation of these two compounds is unnecessary. The methods do not distinguish between the D and L enantiomers of glufosinate ammonium and N-acetyl-glufosinate.

The MARC has subsequently determined that the residues of concern for the currently registered and proposed transgenic and nontransgenic crops are glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517. HED concludes that HRAV-5A is sufficient for enforcement of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 tolerances in/on the registered/proposed nontransgenic crops for the following reasons (no additional validation data are required): **(1)** the analytical procedures for HRAV-5A and BK/01/99 are essentially identical; **(2)** adequate recovery data for N-acetyl-glufosinate using method BK/01/99 as been attained in/on canola (seed, oil, meal), sugar beet (tops, root, dried pulp, molasses, sugar), corn (grain, forage, fodder, meal, flour, starch, oil), soybeans (seed, hay, meal, hull, oil), rice (grain, straw, bran, hull, polished rice), and cotton (seed gin byproducts, oil, hull, meal); and **(3)** based on the currently available metabolism studies, residues of N-acetyl-glufosinate are unlikely in nontransgenic crops.

The analytical methods used in the transgenic cotton and transgenic rice magnitude of the residue and processing studies were similar to method BK/01/95. Since this method has been validated by ACB and adequate validation has been submitted in conjunction with the magnitude of the residue and processing studies, HED concludes that method BK/01/95 is sufficient for enforcement of the rice and cotton tolerances.

The analytical methods used in the field trial and processing studies were similar to the current enforcement methods and are appropriate for data collection purposes.

Livestock: Method HRAV-12 (also known as BK/01/95) has been validated by ACB for determination of glufosinate ammonium and HOE 061517 in/on milk, egg, muscle, and liver (PP# 8F3607, J. Garbus, 26-Oct-1994). Briefly, the method involves extraction with water, protein precipitation with acetone, anion exchange chromatography, derivatization with trimethylorthoacetate, silica gel column clean-up, and quantification via gas chromatography with flame photometric detection (residues expressed as glufosinate free acid equivalents). The method does not distinguish between the D and L enantiomers of glufosinate ammonium.

The MARC has subsequently determined that the tolerance expression for livestock commodities will be for the combined residues of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517. The petitioner submitted a feeding study in which residues of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 were monitored in livestock commodities using method BK/03/95 (method was adequately validated; D211531, M. Rodriguez, 7-Mar-1996). Other than including procedures for quantitation of N-acetyl-glufosinate, method BK/03/95 is identical to the current enforcement method. Since BK/03/95 has been validated for determination of N-acetyl-glufosinate in livestock commodities and the analytical procedure is identical to that of current livestock enforcement method, HED concludes that the current enforcement method is sufficient for enforcement of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 livestock tolerances (no additional validation data are necessary).

860.1360 Multiresidue Methods

Glufosinate ammonium, HOE 061517, and N-acetyl-glufosinate were not quantitatively recovered from any of the FDA Multiresidue Testing Protocols. This information has been forwarded to FDA (PP#8F3607, J. Garbus, 14-Aug-1988; PP#5F4578, M. Rodriguez, 10-Oct-1995).

860.1380 Storage Stability

As part of the current petition, blueberry storage stability data were submitted (45580201.der2.wpd). Control blueberry samples were fortified with glufosinate ammonium and HOE 061517 at 1.00 ppm and placed in frozen storage (<-20 C). The samples were extracted after 615 (glufosinate ammonium) and 593 (HOE 061517) days of storage and the resulting extracts were analyzed 78 (glufosinate ammonium) and 71 (HOE 061517) days after extraction (extracts were stored at <-20 C). The percent recoveries for glufosinate ammonium (95, 96, 98) and HOE 061517 (73, 72, 72) were acceptable.

Previously submitted and reviewed frozen storage stability data indicate that glufosinate ammonium and HOE 061517 are stable for 730 days on frozen apples, corn grain, and soybeans (PP#8F3607, J. Garbus, 8-Aug-1990). Additional storage stability data indicated that glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 are stable for 12 months on transgenic soybean seed, forage and hay; for 3 months on soybean oil and meal; for 6 months on transgenic corn grain, fodder and forage; and for 24 months on transgenic sugar beet tops and roots (D211531 and D219069, M. Rodriguez, 7-Mar-1996; D257629, T. Bloem, 9-Jul-1999).

Based on the available storage stability data and since acceptable percent recoveries were attained for fortified samples run concurrent to the treated samples, HED concludes that the storage intervals and conditions for the samples collected as part of the blueberry, rice, and cotton field trial and processing studies are acceptable.

860.1400 Water, Fish, and Irrigated Crops

In support of the rice Section 3 request, the petitioner submitted a study investigating the quantity of residue in/on crops irrigated with rice paddy water treated with glufosinate ammonium (45204404.der.wpd).

Field trial sites in Rosa, LA and Porterville, CA were planted with transgenic rice and glufosinate ammonium was applied twice at 0.45 lbs ai/acre. In Louisiana, both applications were made to soil and the rice field was flooded 1 day after the second application. In California, both applications were made to a flooded rice field. At both sites, five, eight, and sixteen days after the second application, paddy water was used to irrigate test plots planted with grain sorghum (irrigated 71-88 days after planting), radish (irrigated 9-38 days after planting), collard (Louisiana site only; irrigated 49-60 days after planting), and lettuce (California site only; irrigated 27-38 days after planting).

Irrigated crop samples were collected 14 days after the last irrigation and at maturity and analyzed for residues of glufosinate ammonium and HOE 061517. The analytical method did not distinguish between glufosinate ammonium and N-acetyl-glufosinate (no validation data for N-acetyl-glufosinate was submitted with this study). Residues were generally less <0.008 at both the Louisiana and California test sites. However, residue of glufosinate ammonium was found in/on radish top (<0.008 - 0.014 ppm), radish root (<0.008 - 0.024 ppm), and lettuce (<0.008 - 0.009 ppm) and residues of HOE 061517 were found in/on grain sorghum grain (<0.008 - 0.011 ppm), grain sorghum fodder (<0.008 - 0.008 ppm), and radish top (<0.008 - 0.013 ppm). The petitioner has not provided the storage temperature for the crop samples prior to analysis. These data are necessary to validate the crop residue data. Additionally, HED has determined that the residues of concern in drinking water are glufosinate ammonium, HOE 061517, HOE 064619, and N-acetyl-glufosinate. These residues should have been monitored in the irrigated crops.

Despite the missing data, HED can conclude that residues of glufosinate ammonium and HOE 061517 are possible in/on crops irrigated with rice water paddy water treated with glufosinate ammonium. Therefore, the petitioner should include a statement prohibiting the use of treated rice paddy water for irrigation purposes on the proposed label. **A revised Section B is requested.**

860.1480 Meat, Milk, Poultry, and Eggs

Based on the established/recommended tolerances, the following MTDB were calculated: beef cattle - 15.38 ppm (aspirated grain fractions, corn field forage, cannery waste, cotton gin byproducts), dairy cattle - 15.22 ppm (aspirated grain fractions, corn field forage, cannery waste, cotton gin byproducts), poultry - 3.33 ppm (soybean hulls, soybean meal, soybean seed, cotton meal), and hog - 8.89 ppm (aspirated grain fractions, potato culls, cotton meal, soybean seed). Table 1 is a summary of the MTDB calculations.

Two dairy cow and two poultry feeding studies have been submitted, reviewed, and determined to be adequate: (1) dairy cows and poultry feed a diet containing a 3:1 mixture of glufosinate ammonium and HOE 061517 (PP#8F3607, J. Garbus, 8-Aug-1990) and (2) dairy cows and poultry feed a diet containing a 15:85 mixture of glufosinate ammonium and N-acetyl-glufosinate (D211531, M. Rodriguez, 7-Mar-1996). Two feeding studies were performed on dairy cows and poultry due to the different residues present in transgenic (principally N-acetyl-glufosinate followed by glufosinate ammonium) and non-transgenic crops (principally HOE 061517). The results from the studies are summarized in Tables 2 and 3.

Residues of N-acetyl-glufosinate were not reported in the 3:1 glufosinate ammonium:HOE 061517 dairy cow and poultry feeding studies. Residues of N-acetyl-glufosinate were monitored in the 15:85 glufosinate ammonium:N-acetyl-glufosinate dairy cow and poultry feeding studies. Other than including procedures for quantitation of N-acetyl-glufosinate, the analytical method used in each of the feeding studies were identical. Since the analytical procedures were identical and the livestock metabolism studies indicated that N-acetyl-glufosinate is minor metabolite when livestock are fed glufosinate ammonium, HED concludes that the method used in the 3:1 glufosinate ammonium:HOE 061517 feeding study adequately accounted for N-acetyl-glufosinate.

Table 1: MTDB Calculations

	raw agricultural commodity	tolerance	% DM	% of diet	ppm in diet
beef cattle	aspirated grain fractions	25	85	20	5.88
	corn forage	4.0	40	40	4.00
	cannery waste	4.0	30	35	4.67
	cotton gin byproducts	15	90	5	0.83
	MTDB				15.38
dairy cattle	aspirated grain fractions	25	85	20	5.88
	corn forage	4.0	40	50	5.00
	cannery waste	4.0	30	20	2.67
	cotton gin byproducts	15	90	10	1.67
	MTDB				15.22
poultry	soybean hulls	5.0	90	20	1.11
	soybean meal	2.0	92	40	0.87
	soybean seed	2.0	89	20	0.45
	cotton meal	4.0	89	20	0.90
	MTDB				3.33
hog	aspirated grain fractions	25	85	20	5.88
	potato culls	0.80	20	50	2.00
	cotton meal	4.0	89	15	0.67
	soybean seed	2	89	15	0.34

Ruminant: Lactating cows were orally dosed for 28 days with either a 15:85 mixture of glufosinate ammonium:N-acetyl-glufosinate (9.1 ppm, 27.3 ppm, and 91.1 ppm) or with a 3:1 mixture of glufosinate ammonium:HOE 061517 (4 ppm, 12 ppm, and 40 ppm). Milk samples were collected daily and at sacrifice samples of muscle, liver, fat, and kidney were collected. Table 2 is a summary of the concentrations of glufosinate ammonium, HOE 061517, and N-acetyl-glufosinate found in the collected tissues and milk.

Based on the results of the ruminant feeding studies and the current MTDB for ruminants, HED concludes that the following tolerance for the combined residue of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 are appropriate: meat (cattle, goat, hog, horse, sheep) - 0.15 ppm; meat byproducts (cattle, goat, hog, horse, sheep) - 6.0 ppm; fat (cattle, goat, hog, horse, sheep) - 0.40 ppm; and milk - 0.15 ppm. **A revised Section F is requested.**

Poultry: Laying hens were orally dosed for 28 days with either a 15:85 mixture of glufosinate ammonium:N-acetyl-glufosinate (0.36 ppm, 1.08 ppm, and 3.6 ppm) or with a 3:1 mixture of glufosinate ammonium:HOE 061517 (4.5 ppm, 13.5 ppm, and 45 ppm). Egg samples were collected daily and at sacrifice samples of muscle, liver, fat, kidney (3:1 study only), and skin (15:85 study only) were collected. Table 3 is a summary of the concentrations of glufosinate ammonium, HOE 061517, and N-acetyl-glufosinate found in the collected tissues and milk.

Based on the results of the poultry feeding studies and the current MTDB for poultry, HED concludes that the following tolerances are appropriate: poultry, meat - 0.15 ppm; poultry, meat byproducts - 0.60 ppm; poultry, fat - 0.15 ppm; and egg - 0.15 ppm. **A revised Section F is requested.**

Table 2: Summary of Dairy Cow Feeding Studies

matrix	ppm (glufosinate free acid equivalents)						anticipated residue at 1x MTTDB ¹
	HOE 039866/ HOE 099730 ²	HOE 061517	HOE 039866/ HOE 099730 ²	HOE 061517	HOE 039866/ HOE 099730 ²	HOE 061517	
	15:85 glufosinate ammonium:N-acetyl-glufosinate						
	0.6x MTTDB		1.8x MTTDB		5.9x MTTDB		
milk	<0.02	<0.02	<0.02-0.03	<0.02	0.02-0.23	<0.02-0.03	--, 0.09, 0.04
kidney	<0.10	<0.10	<0.10	<0.10	0.11-0.15	<0.10-0.13	--, --, 0.05
liver	<0.10	<0.10	<0.10	<0.10	<0.10	0.25-0.29	--, --, 0.07
muscle	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	--, --, 0.02
fat	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	--, --, 0.02
	3:1 glufosinate ammonium:HOE 061517						
	0.3x MTTDB		0.8x MTTDB		2.6x MTTDB		
milk	<0.02	<0.05	<0.02	<0.05	<0.02	<0.05	--, --, 0.03
kidney	<0.10	0.41	<0.1	2.0	0.13	7.4	1.70, 2.62, 2.90
liver	0.13	1.5	<0.1	4.2	<0.1	10.7	5.43, 5.38, 4.15
muscle	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	--, --, 0.04
fat	0.06	<0.05	<0.05	0.08	<0.05	0.16	0.37, 0.16, 0.08

¹ anticipated residue based on results from each of the three dosing groups; anticipated residue was not calculated if residues were <LOQ; if residues were <LOQ at all three dosing levels then an anticipated residue was calculated using the results from the highest dose level
² HOE 099730 was not reported in the 3:1 glufosinate ammonium:HOE 061517 feeding study; analytical method would not have distinguished between HOE 039866 and HOE 099730 or the D and L enantiomers of these compounds

Table 2: Summary of Laying Hen Feeding Studies

matrix	ppm (glufosinate free acid equivalents)						anticipated residue at 1x MTDB ¹
	HOE 039866/ HOE 099730 ²	HOE 061517	HOE 039866/ HOE 099730 ²	HOE 061517	HOE 039866/ HOE 099730 ²	HOE 061517	
1.5:85 glufosinate ammonium:N-acetyl-L-glufosinate							
	0.1x MTDB		0.3x MTDB		1.1x MTDB		
liver	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	--, --, 0.18
skin	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	--, --, 0.09
muscle	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	--, --, 0.09
fat	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	--, --, 0.09
egg	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	--, --, 0.09
3:1 glufosinate ammonium:HOE 061517							
	1.4x MTDB		4.0x MTDB		13.2x MTDB		
liver	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	--, --, 0.02
kidney	<0.05	0.69	0.07	2.00	<0.05	7.80	0.53, 0.52, 0.59
muscle	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	--, --, 0.01
fat	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	--, --, 0.01
egg	<0.05	<0.05	<0.05	<0.05	0.07	<0.05	--, --, 0.01

¹ anticipated residue based on results from each of the three dosing groups; anticipated residue was not calculated if residues were <LOQ; if residues were <LOQ at all three dosing levels then an anticipated residue was calculated using the results from the highest dose level

² HOE 099730 was not reported in the 3:1 glufosinate ammonium:HOE 061517 feeding study, analytical method would not have distinguished between HOE 039866 and HOE 099730 or the D and L enantiomers of these compounds

860.1500 Crop Field Trials

Detailed reviews concerning the magnitude of the residue data submitted in support of the current petitions can be found in the following reviews: blueberry (45580201.der1.wpd), transgenic cotton (45089303.der.wpd), and transgenic rice (45204406.der.wpd and 45204407.der.wpd).

Bushberry: The petitioner submitted blueberry magnitude of the residue data conducted in Region 1 (n=1), Region 2 (n=2), and Region 5 (n=2). Rely® (soluble concentrate (SC); 11.33% glufosinate ammonium) was applied twice as a spray directed to the soil at 1.50 lbs ai/acre (1x the maximum proposed single and seasonal application rates; RTI - 25-29 days; spray volumes - 20-31 gallon/acre). Blueberries were harvested at maturity 13-15 days after the final application and analyzed for residues of glufosinate ammonium and HOE 061517 (both expressed as glufosinate ammonium free acid equivalents). The method was adequately validated for data collection purposes (storage interval and conditions have also been validated). Combined residues of glufosinate ammonium and HOE 061517 ranged from <0.03 - 0.08 ppm (residues in/on controls were <0.02). The petitioner has not submitted residue decline data.

HED has determined that the tolerance expression for bushberries will be for residues of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517. Residues of N-acetyl-glufosinate were not monitored in the blueberry magnitude of the residue study. The method used in the blueberry field trials is identical to that used to monitor for residues of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 in the transgenic cotton and transgenic rice studies summarized below. These studies indicate that glufosinate ammonium and N-acetyl-glufosinate are derivatized to the same compound and quantified together. For this reason and since the metabolism studies indicated that residue of N-acetyl-glufosinate are unlikely in nontransgenic crops, HED is willing to conclude that the submitted blueberry field trial data has adequately accounted for residues of N-acetyl-glufosinate in/on blueberry.

Since residues were generally <LOQ, a 25 % reduction in the number of field trials is appropriate. Tables 3 and 5 of OPPTS suggests the submission of the following field trial data when requesting a bushberry crop subgroup tolerance and residues are <LOQ: Region 1 (n=1), Region 2 (n=2), Region 5 (n=2), and Region 12 (n=1). An additional field trial in Region 12 is needed to fulfill the suggested geographical distribution. **Provided the petitioner agrees to conduct a field trial in Region 12 (n=1; residues of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 should be monitored; residue decline data should be included), HED concludes that the available field trial data is sufficient to support a 0.15 ppm permanent tolerance for the combined residues of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 in/on bushberry crop subgroup. A revised section F is requested.**

Transgenic Cotton: The petitioner submitted transgenic cotton magnitude of the residue data conducted in Region 2 (n=1), Region 3 (n=1), Region 4 (n=3), Region 6 (n=2), Region 8 (n=4), and Region 10 (n=3). Each location consisted of a control plot and two treated plots. The 1st treated plot received two over the top broadcast spray applications of glufosinate ammonium at ~0.50 lbs ai/acre (1x and 0.6x the maximum proposed single and seasonal application rates; RTI - 21-53 days). The 2nd treated plot received three applications of glufosinate ammonium at ~0.50 lbs ai/acre with the first and third made using over the top broadcast spray equipment and the second application directed at the bottom third of the plant (1x the maximum proposed single and

seasonal application rates; RTI = 7-28 days). In all cases, glufosinate ammonium was formulated as Liberty™ (water soluble liquid formulation; 18.2% glufosinate ammonium; spray volume - 9-11 gallon/acre). Cotton was harvested by hand (n=6) or mechanically with spindle (n=4) or stripper (n=4) pickers 67-76 days after the last application. Cotton harvested by hand was ginned locally while the mechanically harvested cotton was ginned at Texas A & M University (Bryan, TX). The cottonseed and cotton gin byproduct samples were analyzed for residues of glufosinate ammonium/N-acetyl-glufosinate and HOE 061517 (all expressed as glufosinate ammonium equivalents). The method was adequately validated for data collection purposes (storage interval and conditions have also been validated). Combined residues of glufosinate ammonium/N-acetyl-glufosinate and HOE 061517 in/on cottonseed treated with glufosinate ammonium at ~1.00 lbs ai/acre/season (0.6x) and ~1.50 lbs ai/acre/season (1.0x) ranged from 0.15 - 3.33 and <0.10 - 2.71 ppm, respectively (residues in/on controls <0.05 ppm). Combined residues of glufosinate ammonium/N-acetyl-glufosinate and HOE 061517 in/on cotton gin byproducts treated with glufosinate ammonium at ~1.00 lbs ai/acre/season (0.6x) and ~1.50 lbs ai/acre/season (1.0x) ranged from 0.30 - 7.36 and 0.95 - 11.63 ppm, respectively (residue in/on controls <0.10 ppm; LOQ = 0.10 ppm).

Table 5 of OPPTS suggests the submission of the following field trial data when requesting a cotton tolerance: Region 2 (n=1), Region 4 (n=3), Region 6 (n=1), Region 8 (n=4), and Region 10 (n=3). The geographical distribution of the field trial data is sufficient. HED concludes that the following tolerances are appropriate: cotton, undelinted seed - 4.0 ppm and cotton, gin byproducts - 15 ppm. **A revised Section F is requested.**

Cotton: The petitioner is also requesting hooded spray application to nontransgenic cotton (seasonal total of 1.57 lbs ai/acre). Field trial data depicting only hooded spray applications have not been submitted. Since hooded spray applications are likely to result in residues less than those demonstrated with over the top applications, residue data reflecting only directed applications are unnecessary.

Transgenic Rice: The petitioner submitted transgenic rice magnitude of the residue data conducted in Region 4 (n=9), Region 5 (n=2), Region 6 (n=2), and Region 10 (n=2). Liberty™ (water soluble liquid formulation; 18.2% glufosinate ammonium) was applied twice at 0.45-0.50 lbs ai/acre (1x - 1.1x maximum proposed single application rate) for a seasonal total of 0.88 - 1.02 (1x - 1.2x maximum proposed single application rate (RTI of 12-29 days; spray volume - 10-11 gallon/acre). The applications were either both made to dry ground (n=1), the 1st made to dry ground and the 2nd made to a flooded field (n=7), or both made to a flooded field (n=7). Rice grain and rice straw were harvested at maturity 70-106 days after the final application and analyzed for residues of glufosinate ammonium/N-acetyl-glufosinate and HOE 061517. The method was adequately validated for data collection purposes (storage interval and conditions have also been validated). Combined residues of glufosinate ammonium/N-acetyl-glufosinate and HOE 061517 in/on rice grain and rice straw ranged from <0.10 - 0.74 ppm and <0.10 - 1.48 ppm, respectively (residues in/on controls were <0.05).

The residue decline data indicated that residues of glufosinate ammonium/N-acetyl-glufosinate and HOE 061517 did not significantly change in/on rice grain and rice straw as the preharvest interval (PHI) increased from 78 to 96 days. A side by side comparison concerning the addition of ammonium sulfate (3.36 lbs ai/acre) to the tank mix was performed at three of the field trial

sites. The resulting residue data indicated that the addition of ammonium sulfate to the spray solution did not effect the concentration of glufosinate ammonium/N-acetyl glufosinate and HOE 061517 in/on rice grain and rice straw. Comparable residues were attained when both applications were made to a flooded field (n=6) or the first application was made to a dry field and the second to a flooded field (n=6). Based on the limited field trial data available, both applications applied to a dry field (n=1) may result in lower residues when compared to the other water management practices tested.

Table 5 of OPPTS suggests the submission of the following field trial data when requesting a rice tolerance: Region 4 (n=11), Region 5 (n=1), Region 6 (n=2), and Region 10 (n=2). Two field trials in Region 4 are necessary to fulfill the suggested geographical distribution. Since the petitioner has conducted an additional field trial in Region 5 and conducted side by side comparison concerning the addition of ammonium sulfate at 3 of the field trials (Regions 4, 5, and 6), HED concludes that additional field trial data are unnecessary. Based on the available field trial data, HED concludes that the following tolerances, for the combined residues of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 are appropriate: rice, grain 1.0 ppm and rice, straw - 2.0 ppm. **A revised Section F is requested.**

860.1520 Processed Food and Feed

Detailed reviews concerning the processing studies submitted in support of the current petitions can be found in the following reviews: transgenic cotton (45580201.der.wpd) and transgenic rice (45204406.der.wpd)

Cotton: Transgenic cotton was treated at the 4-leaf and early bloom stages with Liberty™ herbicide (water soluble liquid; 18.2% glufosinate ammonium) at ~2.1 lbs ai/acre (4.29 lbs ai/acre total; 4.8x and 2.7x the maximum proposed single and seasonal application rates, respectively). Cotton was mechanically harvested 76 days after the last application and processed into cottonseed, cottonseed meal, cottonseed hull, and cottonseed refined oil. The processed and unprocessed commodities were analyzed for residues of glufosinate ammonium/N-acetyl-glufosinate and HOE 061517 (analytical method and storage interval and conditions were validated). The resulting residue data indicate that the combined residues of glufosinate ammonium/N-acetyl-glufosinate and HOE 061517 reduced in cottonseed refined oil (0.01x) and concentrated in cottonseed hull (1.2x) and cottonseed meal (1.3x).

Based on the cottonseed highest average field trial (HAFT) of 3.24 ppm from the magnitude of the residue study (45089303.der.wpd); the recommended cottonseed tolerance of 4.0 ppm; and the meal (1.3x), hull (1.2x), and refined oil (0.01x) concentration factors, HED concludes that tolerances for cottonseed processed commodities are unnecessary. Tolerances for cottonseed oil, cottonseed meal, and cottonseed hull will be covered by the unprocessed RAC.

Transgenic Rice: Transgenic rice was treated at the 2-4 leaf stage and the 3-4 tiller stage with Liberty™ herbicide (water soluble liquid; 18.2% glufosinate ammonium) at 2.23 lbs ai/acre (4.47 lbs ai/acre total; 5x the maximum proposed single and seasonal application rates). Rice grain was harvested at maturity 78 days after the last application and processed into rice hull, rice bran, and polished rice. The processed and unprocessed commodities were analyzed for residues of glufosinate ammonium/N-acetyl-glufosinate and HOE 061517 (analytical method and storage

interval and conditions were adequately validated). The resulting residue data indicate that the combined residues of glufosinate ammonium/N-acetyl-glufosinate and HOE 061517 reduced in rice bran (0.8x) and concentrated in rice hull (2.8x) and polished rice (1.3x).

Based on the rice grain HAFT of 0.74 ppm from the magnitude of the residue study (45204406.der.wpd) and the rice hull (2.8x) concentration factor, HED concludes that the following tolerances for the combined residues of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 are appropriate: rice, hulls - 2.0 ppm. **A revised Section F is requested.** Tolerances for rice bran and polished rice will be covered by the unprocessed RAC.

860.1850 and 860.1900 Confined/Field Accumulation in Rotational Crops

A confined rotational crop study has been submitted and reviewed (D211531 and D219069, M. Rodriquez, 7-Mar-1996). Lettuce, radish, and spring wheat were planted 28 and 119 days after the soil was treated with [3,4-¹⁴C]-HOE-039866 at 0.9 lbs ai/acre (0.6x and 1.0x the maximum proposed application rate for cotton and rice, respectively; bushberries are not rotated). All samples planted 28 days after treatment were analyzed. HOE 061517 (5-57% TRR) and HOE 064619 (6-10% TRR) were the only compounds identified (a total of 32-64% of the TRR was identified). Except for the wheat commodities, TRRs were ≤0.02 ppm for the samples planted 120 days after treatment (wheat commodities 0.06-0.15 ppm).

A wheat field rotational crop study has also been submitted and reviewed (P. Errico [RD], 6-May-1998). Wheat was planted 73 - 90 days after the soil was treated with glufosinate ammonium at 0.8 lbs ai/acre (0.5x and 0.9x the maximum proposed application rate for cotton and rice, respectively). Wheat forage, hay, straw, and grain were harvested at maturity and analyzed for residues of glufosinate ammonium and HOE 061517 (residues were < LOQ; LOQ = 0.05 ppm).

Based on the confined and field rotational crop studies, the MARC determined that the residues of concern in rotational crops, for tolerance expression and risk assessment purposes, are glufosinate ammonium, HOE 061517, and HOE 064619 (D282757, T. Bloem, 9-May-2002). The Liberty® label indicates a 120-day PBI for all crops except wheat, barley, buckwheat, millet, oats, rye, sorghum, and triticale where a 70-day PBI is indicated. Based on the results from the confined and field rotational studies, HED concludes that the proposed rotational crop restrictions are appropriate for rice. The currently available confined and field rotational crop studies were conducted at 0.5-0.6x the maximum proposed application rate for cotton. As a result, the magnitude of the residues in/on the rotated crops are not representative of that which would be attained following rotation to a cotton field treated with glufosinate ammonium. Therefore, the petitioner should amend the label indicating that following treatment of cotton with glufosinate ammonium, the field may only be rotated to a registered crop. **A revised Section B is requested.**

Other Considerations

Codex and Mexico do not have maximum residue limits (MRLs) for residues of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 in/on the proposed crops or livestock. Canada does not have MRLs for residues of glufosinate ammonium, N-acetyl-glufosinate, and HOE 061517 in/on the proposed crops, poultry commodities, or milk but does have a MRL of 1 ppm for ruminant liver and kidney. The meat byproduct tolerance determined to be appropriate by HED is greater than the Canadian MRL, therefore harmonization is not appropriate.

Attachment 1: Chemical Structures

Attachment 2: 45204405.der.wpd (transgenic rice metabolism study)

Attachment 3: 45580201.der.wpd (storage stability)

Attachment 4: 45204404.der.wpd (water, fish, irrigated crops)

Attachment 5: 45089303.der.wpd (magnitude of the residue, transgenic cotton)

Attachment 6: 45580201.der.wpd (magnitude of the residue, blueberry)

Attachment 7: 45204406.der.wpd (magnitude of the residue, transgenic rice)

Attachment 8: 45204407.der.wpd (magnitude of the residue, transgenic rice)

Attachment 9: 45089302.der.wpd (processed food/feed, transgenic cotton)

Attachment 10: 45204407.der.wpd (processed food/feed, transgenic rice)

cc with all attachments: T. Bloem (RAB1)

RDI: RAB1 Chemist (19-June-2002)

T. Bloem:806R:CM#2:(703)605-0217:7590C

Attachment 1: Chemical Structures

Chemical Name	Chemical Structure
<p>glufosinate ammonium HOE 039866</p> <p>CAS name - butanoic acid, (±)-2-amino-4-(hydroxymethylphosphinyl)-, monoammonium salt</p> <p>technical is a racemic mixture of the D and L enantiomers</p> <p>analytical method does not distinguish between the enantiomers</p>	
<p>HOE 099730</p> <p>IUPAC name - L-2-acetamido-4-methylphosphinico-butanoic acid</p> <p>analytical method can not distinguish between the D and L enantiomers</p>	
<p>HOE 061517</p> <p>IUPAC name - 3-methylphosphinico-propionic acid</p>	