MEMORANDUM

DATE: 29-JUN-2000

SUBJECT: PP# 8F04973. Review of Proposal to Increase the Tolerance on Field Corn Forage Based on Residues From a New Strain of Roundup Ready® Corn. MRID#: 445313-01. Barcodes D245594 and D245595. Chemical#s 103601and 417300. Case# 289926. Submission# S541598.

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TO: Jim Tompkins/Vickie Walters, PM Team 25
Registration Division (RD) (7505C)

Monsanto Company submitted a petition for increased tolerance levels for residues of the herbicide glyphosate (N-(phosphonomethyl)glycine) in/on field corn forage resulting from the application of Roundup® Ultra to a new strain of Roundup Ready® corn. Monsanto requests modification of the wording of 40 CFR § 180.364(a)(1) to the following: Tolerances are established for residues of glyphosate, (N-(phosphonomethyl)glycine) resulting from the application of the isopropylamine salt of glyphosate and/or the ammonium salt of glyphosate in or on the following raw agricultural commodity (RAC):

Corn, field, forage	3.0 ppm

Currently, as specified in 40 CFR § 180.364(a)(1), tolerances are established for the combined residues of glyphosate (N-(phosphonomethyl)glycine) and its metabolite aminomethylphosphonoic acid (AMPA) resulting from the application of the isopropylamine salt of glyphosate and/or the monoammonium salt of glyphosate in or on the following corn related raw agricultural commodities (RACs):

corn, field, stover ..... 100 ppm
corn, field, forage ..... 1.0 ppm
corn, field, grain ..... 1.0 ppm
poultry, liver ..... 0.5 ppm
poultry, kidney ..... 0.5 ppm
liver* ..... 0.5 ppm
kidney* ..... 4.0 ppm

* Of cattle, goats, hogs, horses, and sheep

Previously submitted residue data (MRID 437127-02) used to set the established glyphosate tolerance levels on corn RACs, were generated with a proprietary line of Roundup Ready® Corn, identified as line 599-04-2, genetically modified to express proteins that confer tolerance to glyphosate. This line expresses both CP4 5-enolpyruvylshikimate-3-phosphate synthase (CP4 EPSPS) and glyphosate oxidoriductase (gox). The CP4 EPSPS enzyme confers tolerance through modification of the glyphosate target-site. The gox enzyme provides a second mechanism of tolerance by converting glyphosate to aminomethylphosphonic acid (AMPA).

Monsanto has developed a second-generation of Roundup Ready® Corn which has been transformed to express a modified version of the wild-type EPSPS enzyme found in corn. This line, identified as GA21, does not express the gox enzyme. Without the gox degradation gene, the primary residue is parent glyphosate. This change in the biochemical processing of glyphosate by the transgenic corn plant has led to the need for additional corn field trials to ensure adequate tolerance glyphosate levels in/on corn RACs.

CONCLUSIONS/RECOMMENDATIONS

HED concludes there are no residue chemistry data requirements that would preclude the proposed increase of the tolerance for glyphosate in/on corn, field, forage. A human-health risk assessment will be prepared as a separate document.

Note to RD: The reference to aminomethylphosphonic acid should be omitted from the tolerance expression, and the prefix "mono" should be removed from "monoammonium".

DETAILED CONSIDERATIONS

Proposed Use: Monsanto Company submitted supplemental labeling for preplant, in crop, and preharvest applications of Roundup® Ultra to corn with the Roundup Ready® gene.

Maximum yearly rates. Preplant: The maximum amount of this product which can be applied prior to crop emergence is 5 quarts per acre. In crop: Sequential in-crop applications of this product from emergence through the V8 stage or 30 inches must not exceed 2 quarts per acre per

growing season. Preharvest: The maximum amount of this product that can be applied after maximum kernel fill is complete and the crop is physiologically mature (black layer formation) until 7 days before harvest is 1 quart per acre. Thus, the combined total per year for all application may not exceed 8 quarts per acre (6 lbs ae/A/year).

Allow a minimum of 50 days between application of this product and harvest of corn forage, and 7 days between application and harvest of corn grain (50 and 7 day preharvest interval (PHI) for corn forage and grain, respectively). Allow a minimum of 10 days between in-crop applications of this product. There are no rotational crop restrictions following applications of this product.

This product may be applied by ground (in 5 - 20 gallons of spray solution per acre) or aerial (in 3 - 15 gallons of spray solution per acre) methods.

Conclusions: The proposed label adequately describes the use of Roundup® Ultra Herbicide on Roundup Ready® corn.

Crop Field Trials: Monsanto Company conducted 22 corn residue field trials during 1997 in AL, GA, IA (3), IL (3), IN, KS (2), MI (2), MN, NE, OH, OK, PA, SD, and WI (3) (see citation shown below). Extensive hurricane damage at the AL site caused the site to be dropped from the study prior to collection of any samples. No grain or stover sample were collected at the OH site due to loss of crop from animal feeding.

MRID 445313-01. M.S. Bleeke, March 1998, Magnitude of Glyphosate Residues in Roundup Ready Corn Raw Agricultural Commodities in the U.S. Following Topical Applications of Roundup Ultra Herbicide. Monsanto report Number MSL-14990, 661 p.

Two corn lines were used in the present study: GA21 and GG25. They both express a modified version of the wild-type EPSPS enzyme and neither contains the gox enzyme or any other enzyme that modifies the metabolic pathway of glyphosate. The GA21 line was used in all 22 field trials, while the GG25 line was used in 6 field trials. The results showed similar residue levels when similar treatment rates were used; however, line GG25 was only subjected to the preemergence and early postemergence applications. Accordingly, only the results for the GA21 line at the maximum application rate are presented in Table 1. Although data were also reported for AMPA, this information was not included in Table 1 because AMPA is not a residue of concern and was only found in small amounts.

Residue decline studies were conducted on corn forage and grain samples. The forage samples demonstrated no discernible residue decline pattern when sampled at 54, 61, 68, and 75 days PHI in Greene, IA, and at 59, 67, 73, and 80 days PHI in Warren, IL. Similarly, the grain samples demonstrated no discernible residue decline pattern when sampled at 88, 95, 102, 109, and 116 days PHI in Greene, IA, and at 101, 108, 115, 122, and 129 days PHI in Warren, IL.

The following glyphosate applications were made: 1) preemergence application - after the seeds

were planted but prior to emergence, 2) early postemergence application - at the V4 - V6 stage, 3) late postemergence application - at the V8 stage or when the plants reached 30 inches in height, whichever came first, and 4) preharvest application - 7 ± 1 days before harvest. Table 1 presents the glyphosate residue levels obtained following all 4 applications, as this pattern led to the highest residue levels. It should be noted that corn forage was harvested prior to the preharvest application.

Table 1. Residues of Glyphosate in/on Roundup Ready® Corn Forage, Grain, and Stover in Line GA21.

Location	EPA Region	Total Rate (lb ae/A)[a]	PHI (days)	Glyphosate Residue (ppm)		
				Forage	Grain	Stover
Pulaski, GA	2	5.65, 0.73, 0.74, 0.75	47, 7, 7	**2.23**, 2.08	0.16, 0.16	**31.1**, 24.6
Jefferson, IA	5	5.70, 0.74, 0.69, 0.74	66, 8, 8	0.22, 0.25	0.19, 0.09	1.93, 2.50
Hamilton, IA	5	4.95, 0.76, 0.75, 0.76	59, 7, 7	0.80, 0.69	0.14, 0.10	5.18, 3.47
Greene, IA	5	5.66, 0.84, 0.75, 0.75	61, 7, 7	1.19, 0.97	0.22, 0.18	22.6, 22.5
Jersey, IL(1)	5	5.75, 0.76, 0.76, 0.75	43, 8, 8	2.13, 1.96	0.18, 0.16	5.08, 5.05
Jersey, IL(2)	5	6.31, 0.74, 0.73, 0.78	49, 7, 7	1.94, 1.86	0.19, 0.17	8.76, 8.20
Warren, IL	5	5.41, 0.75, 0.81, 0.85	67, 14, 21	1.40, 1.16	**0.27**, 0.17	6.59, 4.40
Hamilton, IN	5	5.91, 0.77, 0.75, 0.78	64, 7, 7	1.68, 1.50	0.07, 0.06	4.20, 3.58
Sedgwick, KS	5	5.44, 0.76, 0.75, 0.75	52, 11, 13	1.66, 1.63	0.16, 0.13	6.39, 5.70
Kingman, KS	5	5.87, 0.74, 0.78, 0.74	51, 10, 10	0.95, 0.80	0.07, 0.06	2.41, 2.22
Ingham, MI	5	5.81, 0.75, 0.76, 0.74	77, 6, 6	0.56, 0.37	0.06, 0.06	4.64, 3.49
Ottawa, MI	5	5.55, 0.74, 0.74, 0.75	74, 7, 7	0.31, 0.30	0.04, 0.03	5.46, 5.17
Traverse, MN	5	5.70, 0.75, 0.75, 0.73	60, 7, 7	1.18, 1.11	0.15, 0.14	19.3, 17.1
York, NE	5	5.73, 0.77, 0.77, 0.78	60, 7, 7	0.30, 0.28	0.26, 0.21	2.60, 2.25
Fayette, OH	5	6.47, 0.75, 0.74	64	0.27, 0.21	NA[b]	NA[b]
Caddo, OK	6	5.67, 0.77, 0.76, 0.76	42, 7, 7	0.82, 0.75	0.05, 0.05	23.8, 17.5
Berks, PA	1	5.87, 0.79, 0.74, 0.74	76, 7, 7	0.41, 0.39	0.03, 0.03	2.89, 2.18
Marshall, SD	5	5.69, 0.74, 0.75, 0.75	56, 7, 7	1.32, 1.15	0.15, 0.15	3.58, 3.12
Dane, WI	5	5.23, 0.67, 0.73, 0.71	69, 7, 7	0.36, 0.32	0.06, 0.05	17.0, 14.5
Walworth,	5	5.65, 0.76, 0.76, 0.76	65, 7, 7	0.91, 0.52	0.05, 0.04	3.15, 2.99

WI						
Pepin, WI	5	5.76, 0.74, 0.76, 0.77	72, 7, 7	0.09, 0.08	0.01, 0.01	1.51, 1.45

[a] Application rates listed are for preemergence, early postemergence, late postemergence, and preharvest applications, respectively.
[b] Sample not collected because of crop damage from animals.

All samples were analyzed using high performance liquid chromatography (HPLC) with fluorometric detection. This method has undergone successful Agency validation and was recommended for inclusion in PAM II (Memo, R. Perfetti, 27-OCT-1992). The reported limit of quantitation (LOQ) for corn forage, grain, and stover was 0.04, 0.04, and 0.06 ppm, respectively. The reported results were not corrected for concurrent recovery data, which were mostly within a range of 60 - 120%.

The maximum interval between sampling and extraction for the corn samples was as follows: 109 days for forge, 78 days for grain, and 141 days for stover. The stability of glyphosate in or on frozen crop samples has been previously determined to be at least 2.5 years (MRID 414720-02).

Conclusions: The number and geographical distribution of corn field trials is adequate. The available crop field trial data depicting glyphosate residues in the GA21 line of Roundup Ready® Corn support the established tolerances of 1.0 and 100 ppm for corn grain and stover, and support a new tolerance of 3.0 ppm for corn forage.

Meat, Milk, Poultry, and Eggs: Because of the many potential feed items for which glyphosate tolerances are established, recent glyphosate reviews have made use of more realistic livestock diets to estimate dietary burdens (D201255, M.I. Rodriguez, 12-JAN-1995; and D238398, J. Garbus and T. Morton, 18-SEP-1998). Most recently, dietary burdens of 210 and 220 ppm were estimated for dairy and beef cattle, respectively (D256740, W. Donovan, 09-JUN-2000). These dietary burdens included a contribution from alfalfa hay as the roughage component of the diet, with a tolerance of 400 ppm. Comparison of the resulting dietary burden to available residue levels from cattle, hog and hen feeding studies demonstrated that existing glyphosate tolerance levels for all livestock liver and kidney (except poultry) are adequate, but that tolerance levels of 0.30 and 1.0 ppm are needed for egg and poultry meat byproducts, respectively. As the current proposal is to increase the established corn, field, forage tolerance from 1.0 to 3.0 ppm, no increase in the dietary burden to cattle is expected to result from approval of the present action. Additionally, no impact is expected on the dietary burden to poultry or hogs since corn forage is not a feed item for these livestock.

Conclusions: Existing and proposed glyphosate tolerances on meat, milk, poultry, and eggs are adequate to cover the proposed tolerance increase in/on corn, field, forage.

cc: W. H. Donovan, H. Jamerson (RD)
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