

APR 10 1981

Memorandum

SUBJECT: PP25F2422. Glyphosate on forage leucines and grasses.
Evaluation of analytical methods and residue data.

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Persanto requests the establishment of tolerances for combined residues of the herbicide glyphosate (N-(phosphonomethyl)glycine) and its metabolite aminomethylphosphonic acid in or on the raw agricultural commodities forage leucines and forage grasses at 0.1 ppm and 0.2 ppm respectively.

Tolerances for glyphosate have been established on a variety of commodities. These tolerances range from 0.1 to 15 ppm.

Other glyphosate petitions pending include OE2379, OE2421, 1E2443, 1E2444 and 1E2455.

Conclusions

- 1A. The nature of the residue in plants and animals is adequately understood. The terminal residue will consist of glyphosate and aminomethylphosphonic acid.
- 1B. Contaminant glyphosate (CGP) is an impurity in both the formulated and technical product. The presence of this impurity however, has undergone a hazard evaluation with the result that CGP is not barring the establishment of glyphosate tolerances because of the presence of this material.
2. Adequate analytical methods are available for enforcement of the proposed tolerances.

- 3a. Combined residues of glyphosate and aminomethylphosphonic acid would not be expected to exceed 0.2 ppm in forage grasses and 0.4 ppm in forage legumes.
- 3b. Since higher tolerances have been established earlier for soybeans (6 ppm), soybean forage and soybean hay (15 ppm) and since tolerance proposals of 0.3 ppm for peanut forage, 0.4 ppm for peanut hulls and 0.1 ppm for peanuts are pending but currently in reject status revised Sections B and F will be required. In the revised Section F the tolerance regulation should be proposed in terms of "Forage legumes (except soybeans and peanuts)". The revised Section B should contain label directions allowing treatment of "Forage legumes (except peanuts)". The modified Section B should also state that only one pre-emergence application per year is to be made to forage grasses and legumes. Since the use will be for a pre-emergence treatment use we consider the 8 week PHI prescribed on the label to be practical.
- 4a. Secondary residues of glyphosate and/or its metabolite which may result in the liver and kidney of livestock will be covered under the existing tolerance for these commodities.
- 4b. Glyphosate continues to be classed in category 3 of Section 180.6(a) for the commodities milk, eggs, and other animal tissues. This conclusion is based on the feeding studies submitted and the proposed tolerance levels.
5. The International tolerance sheet is attached. There are no proposed Codex tolerances for residues of glyphosate and aminomethylphosphonic acid of forage grasses and legumes. There are however Canadian tolerances at a level of 0.1 ppm on these commodities. These Canadian tolerance regulate the parent compound only. They would not be compatible with the higher U.S. tolerances which regulate combined residues of parent and metabolite. Also, residue data for Canada have been submitted and these data indicate that residues of either parent and/or combined residues of parent and aminomethylphosphonic acid may exceed 0.1 ppm on forage grasses and legumes.

Recommendations:

We recommend that the proposed tolerances not be established for the reasons given in conclusion 3b. Requirements for resolution of the deficiencies stated in conclusion are discussed therein. The petition should be informed of these requirements.

We note that TOI has objected to these and other glyphosate tolerances until questions concerning impurities in the formulation are resolved (Memo of 2/5/81, W. Nykstra).

Note to the PH: When and if these tolerances are established the tolerances for forages and hay of seed and pod vegetables can be deleted from 40 CFR 180.364 since these r.s.c.'s will be covered under the forage legume tolerances.

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DETAILED CONSIDERATIONSFormulation:

The formulation requested for use on forage grasses and legumes is Monsanto's Roundup Herbicide. This formulation contains 41% of the isopropylamine salt of glyphosate and is marketed as an aqueous concentrate (EPA Reg. No. 524-300). The concentrate contains 3 lb of the acid/gallon (4 lb of the isopropylamine salt/gallon).

All inert ingredients in the formulation are cleared under Section 180.1001.

The manufacturing process for technical glyphosate was submitted in conjunction with PP/EF1203. The process was discussed in detail in our review of PP/681026/FA/7525140. Technical glyphosate contains 10% (maximum) impurities which were recently listed in our review of PP/792159. We expect no residue problem with these impurities in the formulation.

Nitrosonglyphosate has also been found in the Roundup formulation and in the technical material. This material has undergone an evaluation of hazard, with the result that OPP is not stopping the establishment of glyphosate tolerances because of the presence of N-nitrosonglyphosate (see memo of 8/24/78, R. Taylor to, E.L. Johnson and 5/5/78 memo for records R. Taylor).

Proposed Use

The proposed use on forage grasses and legumes calls for application of up to 3.75 lb acid equivalent/acre to forage grasses and legumes. A maximum of 6 lb acid equivalent/acre-year is to be applied. An 8 week PHI for feeding an foraging treated crop is prescribed. We will discuss the practicality of this PHI in the Residue Section below.

Nature of the Residue:

No new metabolism studies were submitted in this petition. Metabolism studies on a variety of crops (corn, soybeans, wheat, cotton, rice, barley, oats, sorghum, sugarbeets, sugarcane, potatoes, vegetable crops, grapes, coffee and citrus fruits) have been submitted in previous petitions. These metabolism studies have demonstrated that glyphosate is not readily absorbed from the soil via the root system of plants. Translocation does occur when the compound is applied to aerial plant parts. Metabolism occurs slowly in plants, for example, after 4-7 weeks 90% of the total material applied to apples was parent compound while metabolites aminomethylphosphonic acid and methylaminomethylphosphonic acid comprised 6% of the total residue. Degradation occurs by C-H bond cleavage to form aminomethylphosphonic acid and glyoxylate which are further catabolized with subsequent incorporation into natural plant constituents.

Metabolism studies in rats, rabbits and cows indicated that parent compound makes up the major portion of the residue in mammals with only trace amounts of aminomethylphosphonic acid being observed.

The nature of the residue in plants and animals is adequately understood. The terminal residue will consist of parent and aminomethylphosphonic acid.

Analytical Method:

The analytical method used to determine residues of glyphosate and aminomethylphosphonic acid in forage grasses and legumes is essentially the PAM II method. The method has previously undergone a successful method trial on soybeans and beef liver (PPAF1536). Although the method is time-consuming RCR, after consultation with the FDA, has concluded that it is adequate for enforcement purposes (memo of 1/6/77, J.G. Cunnings). Briefly, the method involves extraction with water followed by isolation of parent and metabolite via ion exchange chromatography. The compounds are then converted to their corresponding di-trifluoromethyl derivatives and determined via dlc using a phosphorous specific flame photometric detector. Certain samples may require additional column clean-up.

Validation data submitted in this petition for forage grasses and legumes reflected fortification of these commodities with glyphosate or aminomethylphosphonic acid at levels of 0.05 to 0.9 ppm. Recoveries of parent and metabolite ranged from 43 to 109% and 43 to 115% respectively. Blank crop values ranged from 0.05 to 0.17 ppm in forage grasses and from 0.05 to 0.05 ppm in forage legumes.

A recently submitted hplc method for parent compound and metabolite has undergone successful method trial on peanuts (memo of P.W. Storrer, PPAF2329, 1/19/81). An earlier method has also been successfully tried on tomatoes and cottonseed (PPAF2444, memo of 9/19/80, R.W. Storrer). This method determined glyphosate only. The two hplc methods are not considered to be as sensitive as the current method of enforcement although they are less time consuming. These methods are suitable for confirmatory analyses.

Adequate analytical methods are available for enforcement of the proposed tolerances.

Residue Data

Residue data submitted in this petition was reviewed previously in conjunction with PP#262080 (M. Holson, 9/22/74). In addition to the data submitted the petitioner has referenced data in EPA's 1536, 1984 and 2329 for grain crops, alfalfa and peanuts respectively. We have also considered appropriate residue data in other petitions for tolerances (either temporary or permanent) on the crops in the forage grasses and legumes groups. Based on data submitted to date it is our judgment that combined residues of glyphosate and aminomethylphosphonic acid would not be expected to exceed 0.2 ppm in forage grasses and 0.4 ppm in forage legumes. The petitioner should be informed however that we will require revised Sections B and F excluding peanuts from the label for forage legumes and excluding soybeans and peanuts from the tolerances expression. That is the label directions should read "forage legumes (except peanuts)" and the proposed tolerance expression should be stated in terms of "forage legumes (except soybeans and peanuts)". This is needed because higher tolerances have been established previously for soybean forage and hay (15 ppm) and tolerance proposals of 0.3 ppm for peanut forage, of 0.4 ppm for peanut hulls and of 0.1 ppm for peanuts are pending but currently in reject status. The revised Section B should also propose a statement clarifying that application of glyphosate to forage grasses and legumes must be made pre-emergence. Since the use will be for a pre-emergence treatment, we consider the 8 week PHI prescribed on the label to be practical.

Note to the PIR: When and if these tolerances are established the tolerances for forage and hay of seed and pod vegetables can be deleted from 40 CFR 100.304 since these r.a.c.'s will be covered under the forage legume tolerances.

Milk, Poultry and Eggs:

Forage grasses and legumes are major cattle feed items. Feeding studies submitted previously in conjunction with PP#-F1536 and reviewed therein reflected feeding a 3:1 ratio of glyphosate and aminomethylphosphonic acid to cattle, poultry and swine for 30 days at levels of 10, 30 and 100 ppm. Based on these studies EPA has concluded earlier that the established tolerances on the kidney and liver of livestock would be adequate to accommodate a 4 ppm dietary level in livestock. This level is significantly higher than the 0.4 (or 0.2) ppm level proposed for forage legumes (or grasses) and therefore we conclude that any residues resulting in liver or kidney from this use of glyphosate will be covered under the existing tolerances.

Based on the feeding studies submitted previously and the proposed tolerance level this compound continues to be classed in category 3 of Section 150.6(a) with respect to milk, eggs and other animal tissues.

Other Considerations:

The International tolerance sheet is attached. There are no proposed Codex tolerances for residues of glyphosate and aminomethylphosphonic acid in forage grasses and legumes. There are however Canadian tolerances for these commodities (0.1 ppm) which regulate parent compound only. We do not find that the proposed U.S. tolerances could be made compatible with these Canadian tolerances especially since we have Canadian data which indicates both that the residues of parent and combined residues of parent and metabolite on these commodities may be greater than 0.1 ppm.

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cc: RF, Circ., Perfetti, Watts, FDA, TOX, EEB, EFB, PP:GF2422
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