

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

FEB 20 1981

DATE

SUBJECT PP#1G2440. Glyphosate on cottonseed. Evaluation of analytical methods and residue data.

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TO Robert Taylor, PM 25
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and

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Monsanto Company, Agricultural Products Division requests a temporary tolerance for the combined residues of the herbicide N-(phosphonomethyl)-glycine (glyphosate) and its metabolite, aminomethylphosphonic acid, in or on the r.a.c. cottonseed at 15.0 ppm. This tolerance is to cover residues resulting from a preharvest topical treatment (plus the already registered preplant use).

Tolerances are established for glyphosate and its metabolite on grain crops at 0.1 ppm, forage grasses at 0.2 ppm, soybeans at 6.0 ppm and soybean forage and hay at 15.0 ppm (40 CFR 180.364). In addition, a tolerance of 6.0 ppm is established on cottonseed.

Petitions pending or under review are OE2421 (cranberries), 1E2448 (papaya), 1E2443 (guaya), OF2422 (forage grasses and legumes) and OF2329 (peanuts, awaiting MTO for favorable recommendation).

The EUP requested in conjunction with this temporary tolerance is for treatment of ca. 640 acres with 1344 lb. active glyphosate (acid equivalent) for each of two years.

CONCLUSIONS

1. The nature of the residue in both plants and animals is adequately understood.
2. Adequate analytical methodology is available to enforce the proposed temporary tolerance.
- 3a. The proposed 15.0 ppm tolerance for residues of glyphosate and its metabolite, aminomethylphosphonic acid, is adequate to cover residues likely to result from the proposed use.

3b. The feeding restrictions on the proposed label make tolerances for cotton forage and hay unnecessary.

3c. Temporary food additive tolerances are not necessary for the by-products of cottonseed processing.

4a. Secondary residues of glyphosate and its metabolite, aminomethylphosphonic acid, in the liver and kidney of cattle, goats, hogs, horses, poultry and sheep resulting from the proposed use may exceed the established tolerance of 0.1 ppm. A temporary tolerance of 0.5 ppm would be more appropriate.

4b. There will be no problem with secondary residues in meat (except liver and kidney), milk and eggs (Section 180.6(a)(3) applies).

RECOMMENDATIONS

We recommend against the proposed tolerance for the reason cited in Conclusion 4a. In addition, we defer to TOX as to the necessity for obtaining the information regarding the dioxane content of the formulated product which was requested in their memo of 12/4/80 (G. Burin).

DETAILED CONSIDERATIONS

Manufacture and Formulation

Glyphosate is formulated as Roundup, an aqueous concentrate which contains 41% of the isopropylamine salt per gallon (4 lb per gallon of the isopropylamine salt, equivalent to 3 lb per gallon glyphosate acid).

The adjuvant, [REDACTED] is cleared under 40 CFR §180.1001.

According to TOX (memo of G. Burin, 12/4/80), Monsanto has submitted Sec.6(a)(2) information (letter of 11/17/80) indicating that the surfactant used in the Roundup formulation contains [REDACTED] but the name of the surfactant and the level of [REDACTED] were not given. [REDACTED] is cleared under 40 CFR 180.1001(d). We defer to TOX for determination of the necessity for obtaining this information.

N-nitrosoglyphosate (NNG) is reported as an impurity in both the technical and the formulated products (Roundup); levels in the formulated product are 0.2-0.4 ppm (see memo of M. Nelson, 5/30/80, PP#OF2329). NNG was subjected to hazard assessment review (see memo of T. Taylor, FHS to DAA, OPP dated 8/24/78). It was concluded that we do not bar establishment of glyphosate tolerances for this reason (see memo of Taylor, 9/5/78).

MANUFACTURING/INERT INGREDIENT
INFORMATION DELETED

This petition contains residue analyses for NNG in cottonseed, levels are all reported as <0.10 ppm.

Proposed Use

For pre-harvest topical applications, apply 0.375 - 4.5 lb a.i.(acid)/A in 5 to 50 gal/A by ground equipment or 1 to 10 gal/A aerially. Add 0.5% (by volume) approved nonionic surfactant if desired.

Apply to non-irrigated cotton after 80% of bolls are opened or, for irrigated cotton, after 70% are open. Do not graze treated fields, do not feed treated foliage and do not apply to crops grown for seed. This gives a very short PHI (1-2 days).

Currently registered uses of glyphosate on cotton are a preplant use of 3.75 lb a.i.(acid)/A and a recirculating sprayer treatment using 3 lb a.i.(acid)/A. A 7 day PHI is associated with the recirculating sprayer treatment, and a complete restriction against feeding or grazing treated cotton plants is currently imposed.

Nature of the Residue

The ¹⁴C - labelled glyphosate plant metabolism studies were reviewed in connection with PP#4G1444 (D. Duffy, 6/3/74); studies are available on corn, wheat, cotton and soybeans. These studies indicate that only limited uptake from the soil occurs, and that once in the plant, glyphosate is metabolized to aminomethylphosphonic acid and glyoxalate, further metabolized and the fragments reincorporated into natural plant constituents.

A study on coffee was reviewed in PP#6F1798 which showed that foliar application results in rapid translocation accompanied by very little degradation.

The residue of concern in plants is comprised of glyphosate and its metabolite, aminomethylphosphonic acid.

Animal metabolism studies were also reviewed in PP#4G1444, and the major component of the residue was found to be the parent compound. The metabolism in animals is considered to be adequately defined for the purposes of this temporary tolerance.

Analytical Methodology

The analytical method used to obtain the residue data submitted with this petition is the somewhat laborious GLC method which has been reviewed and accepted in previous requests for cotton tolerances (PP#1G1444, 6G1757 and 7F1971) and is reviewed in detail in PP#5F1536 (M. Nelson, 3/7/75). A successful tryout was performed on soybeans (memo of K. Zee, 11/1/75, PP# 5F1536).

In PP#6F1798 (memo of M. Nelson, 9/15/76), low-level recovery data were

reported. At fortification levels of 0.05 to 0.4 ppm, recoveries were 60-100% for parent glyphosate and 71-101% for the metabolite aminomethylphosphonic acid in cottonseed; 51-90% for parent and 51-104% for the metabolite in cotton forage and hay; and 46-100% for parent and 55-94% for the metabolite in gin trash.

Recovery data submitted in this petition indicate that at fortification levels of 0.05 to 0.4 ppm, recoveries were 56.7-68% for parent and 63.4-93.2% for the metabolite in cottonseed. At the same levels, recoveries were 66.3-89.4% for parent and 66-84.9% for metabolite in cotton hay. Recoveries of N-nitrosoglyphosate at fortification levels of 0.1-0.2 ppm were 62-65.3% for cottonseed and 71-72.8% for cotton hay.

We conclude that the available analytical methodology, although time-consuming, is adequate to enforce the proposed temporary tolerance.

Residue Data

Twelve residue studies reflecting topical application of glyphosate to cotton are submitted; of these, six plots received the registered pre-emergent ground application, and three of these also received treatments with a recirculating sprayer system. Residue levels are corrected for average recoveries.

Of the six studies which received only topical application (4.5 lb a.i./A), residue levels of glyphosate in the cottonseed ranged from a low of 0.10 ppm at 0 days PHI to a maximum of 6.96 ppm at 3 days PHI. PHI's were up to 14 days. Residue levels of aminomethylphosphonic acid ranged from a low of <0.05 ppm at 0 days PHI to 0.31 ppm at 10 days PHI, and residues of N-nitrosoglyphosate were non-detectable in all samples (<0.10 ppm).

Three studies received a preplant application of 8 lb a.i./A plus topical application of 4.0 lb a.i./A and were sampled at 9 or 13 days PHI. Residue levels of glyphosate in the cottonseed ranged from 0.72-6.47 ppm, and levels of aminomethylphosphonic acid ranged from <0.05-0.08 ppm. Residues of N-nitrosoglyphosate were not reported.

Three more studies received preplant application of 8 lb a.i./A, topical application of 4.0 lb a.i./A and either 1, 2 or 3 applications using a recirculating sprayer system (6 or 10.6 lb a.i./A/application). Total dosages ranged from 24-30.6 lb a.i./A, and residue levels of glyphosate in the cottonseed were 3.09-9.33 ppm at 9-13 days PHI. Residue levels of aminomethylphosphonic acid ranged from <0.05-0.11 ppm and levels of N-nitrosoglyphosate were not reported. (These residue values are corrected for the average % recovery as given on p. D-10; explanation of data calculations by D. Richardson, Monsanto to R. Quick, RCB on 2/13/81.)

The requested temporary tolerance level of 15.0 ppm will be adequate to cover residues of glyphosate and its metabolite, aminomethyl phosphonic acid, which are likely to result from the proposed use (including already registered uses of Roundup). This tolerance level may be somewhat higher than necessary; however, for the purposes of this temporary tolerance, we are not requesting a lower level.

Residue levels in cotton hay are reported for the same studies. Of the six studies receiving single applications, glyphosate residues were 5.01-174.6 ppm and residues of aminomethylphosphonic acid were 0.10-1.24 ppm. Residues of N-nitrosoglyphosate were non-detectable in all samples.

Of the samples receiving both preplant and topical applications, residue levels of glyphosate in the cotton hay were 20.27-46.21 ppm and residue levels of aminomethylphosphonic acid were 0.13-0.26 ppm. In the samples receiving preplant and topical applications plus 1-3 treatments with the recirculating sprayer system, residue levels of glyphosate were 10.01-51.33 ppm and levels of aminomethyl phosphonic acid were 0.12-0.38 ppm. Levels of N-nitrosoglyphosate were not reported.

No tolerance for cotton hay is requested, although residue data are available. The proposed feeding restrictions in Section B are adequate to ensure that temporary tolerances for hay and forage are not required.

A cottonseed processing study was reviewed in PP#7F1971 (D. Duffy, 12/2/77) in which seed having total residues of 1.6 ppm were fractionated into hulls, meal and oil. In all commodities, residue levels were lower than in the seed; no data for soapstock were submitted. In our later review of the same petition (M. Nelson, 3/28/78), we discussed the maximum theoretical residue levels which could be in the soapstock, based on the percentage of free fatty acids in the oil versus that in the soapstock. We then concluded that the maximum residue levels in cottonseed soapstock would be about 50X that in the oil (which was non-detectable, <0.05 ppm). For the purposes of this temporary tolerance, we conclude that no temporary food additive tolerances are necessary at this time.

Meat, Milk, Poultry and Eggs

Cottonseed may comprise up to 25% of the diet of beef cattle. Feed use of cotton forage and hay are restricted on the proposed label. Other feed items bearing glyphosate residues are soybean forage and hay (15.0 ppm, 40% of the diet), soybeans (6.0 ppm, 25% of the diet) and forage grasses (0.2 ppm, 70% of the diet). Thus, dietary intake levels for cattle might be as high as ca. 12 ppm. Since cottonseed meal may comprise up to 25% of the poultry diet, the dietary intake of poultry is calculated to be ca. 1.5 ppm.

Feeding studies on cattle, poultry and swine were reviewed in PP#7F1971 (D. Duffy, 12/2/77). Levels of 10, 30 and 100 ppm in the diet were fed, and a 3:1 ratio of glyphosate:aminomethylphosphonic acid was used. At the 100 ppm feeding level, no detectable (<0.025 ppm) residues of glyphosate or its metabolite were found in milk or eggs and none (<0.05 ppm) were found in the muscle or fat of cattle, swine or poultry. Residues were detected in liver and kidney with the highest levels in kidney. Residues were detected in kidney of cattle and swine at all feeding levels (the 10 ppm level in cattle was not analyzed). In cattle at the 30 and 100 ppm dietary levels respectively, residues of parent were 0.67 and 1.18 ppm and residues of metabolite were 0.13 and 0.46 ppm; residues were <0.05 ppm after 30 days withdrawal. Residues of parent glyphosate in swine kidney were 0.11, 0.42 and 0.93 ppm at the 10, 30 and 100 ppm feeding levels, respectively; residues of metabolite were detectable only at the

100 ppm feeding level and were 0.20 ppm. Residues declined in swine kidney, but were still at detectable levels after the 30 day withdrawal period.

At the higher dietary intake now indicated, the established tolerance of 0.1 ppm for residues of glyphosate and its metabolite, aminomethylphosphonic acid, in the liver and kidney of cattle, goats, hogs, horses, poultry and sheep is no longer considered adequate. A temporary tolerance of 0.5 ppm would be more appropriate.

The absence of detectable residues in meat (except liver and kidney), milk and eggs at 100 ppm in the diet places this use in Category 3 of 180.6(a) with respect to these commodities.

cc: Reading file
Circu
Reviewer
FDA
PP# No.
TOX
EEB
EFB
Randy Watts

TS-769:Reviewer:LMBradley:LMBradley:CM#2:RM:810:Date:1/13/81

LDT:Date:2/18/81

RDI:Section Head:RJH:Date:2/21/81:RDS:Date:2/17/81

File last updated 1/21/81

ACCEPTABLE DAILY INTAKE DATA

RAT, Older NOEL	S.F.	ADI	MPI
mg/kg ppm		mg/kg/day	mg/day (60kg)
5.000 100.00	100	0.0500	3.0000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Grain Crops (64)	0.100	13.79	0.02069
Avocados (6)	0.200	0.03	0.00009
Citrus Fruits (33)	0.200	3.81	0.01144
Coffee (36)	1.000	0.75	0.01119
Cottonseed (41)	6.000	0.15	0.01350
Grapes, inc raisins (66)	0.100	0.49	0.00074
Leafy Vegetables (80)	0.200	2.76	0.00828
Molasses (96)	2.000	0.03	0.00092
Nuts (101)	0.200	0.10	0.00031
Pome Fruits (126)	0.200	2.79	0.00837
Root Crop Veg (138)	0.200	11.00	0.03299
Seed&Pod Veg (143)	0.200	3.66	0.01098
Soybeans (148)	6.000	0.92	0.08263
Palm Oil (202)	0.100	0.03	0.00005
Kidney (203)	0.100	0.03	0.00005
Pistachio nuts (210)	0.200	0.03	0.00009
Liver (211)	0.100	0.03	0.00005
Sugar, cane&beet (154)	0.100	3.64	0.00546
Asparagus (5)	0.200	0.14	0.00043
Bananas (7)	0.200	1.42	0.00426
Olives (104)	0.100	0.06	0.00009
Stone Fruits (151)	0.200	1.25	0.00374

MPI	TMRC	% ADI
3.0000 mg/day (60kg)	0.2163 mg/day (1.5kg)	7.21

Unpublished, Tox Approved PP#8E2122, 9H5196, 9F2163, 9H5204, 0F2329

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Sugar, cane&beet (154)	1.900	3.64	0.10369
Molasses (96)	18.000	0.03	0.00828
Cucurbits (49)	0.100	2.84	0.00426
Fruiting Vegetables (60)	0.100	2.99	0.00449
Small Fruit, berries (146)	0.100	0.83	0.00124
Hops (73)	0.100	0.03	0.00005
Fish, shellfish (59)	2.000	1.08	0.03250
Potable Water (198)	0.100	133.33	0.20000
Peanuts (115)	0.100	0.36	0.00054

MPI	TMRC	% ADI
3.0000 mg/day (60kg)	0.5714 mg/day (1.5kg)	19.05

Current Action PP# 0E2421

CROP
Cranberries (

Tolerance Popa factor mg/day (60kg)
0.200 0.03 0.00009

MPI
3.0000 mg/day (60kg)

TMRC
0.5714 mg/day (1.5kg)

% ADI
19.05
