

US EPA ARCHIVE DOCUMENT

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE FEB 20 1981

SUBJECT PP#1F2455. Glyphosate on cottonseed. Evaluation of analytical method and residue data.

FROM Lynn M. Bradley, Chemist
Residue Chemistry Branch (TS-769) *Lynn M. Bradley*

TO Robert J. Taylor, PM Team 25
Fungicide-Herbicide Branch
Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

THRU: Charles L. Trichilo; Chief
Residue Chemistry Branch (TS-769) *C. L. Trichilo*

Monsanto Company, Agricultural Products Division requests a tolerance for combined residues of the herbicide N-phosphono-methylglycine (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 uses).

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.

Petition 1G2440 requesting a temporary tolerance of 15.0 ppm on cottonseed is currently under review.

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

CONCLUSIONS

1. The nature of the residue in both plants and animals is adequately understood. The residue of concern is the parent plus the metabolite aminomethylphosphonic acid.
2. Adequate analytical methodology is available to enforce the proposed tolerance.
- 3a. The proposed 15.0 ppm tolerance for residues of glyphosate and its metabolite, aminomethylphosphonic acid, is adequate to cover residues resulting from the proposed use.
- 3b. Food additive tolerances for the processed commodities derived from cottonseed are not required.
- 3c. Either a tolerance proposal or a total restriction against feeding treated forage and hay is needed. An appropriate tolerance level would be 15 ppm.

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 use proposed in this petition may exceed the established tolerance of 0.1 ppm. An appropriate tolerance level for the liver and kidney of cattle, goats, hogs, horses, poultry and sheep would be 0.5 ppm. A revised Section F should be submitted.

4b. There will be no problem with secondary residues in meat, fat and meat by-products (except liver and kidney) of cattle, goats, hogs, horses, poultry and sheep and in eggs and milk from the proposed and established glyphosate tolerances (Sec. 180.6(a)(3)).

RECOMMENDATIONS

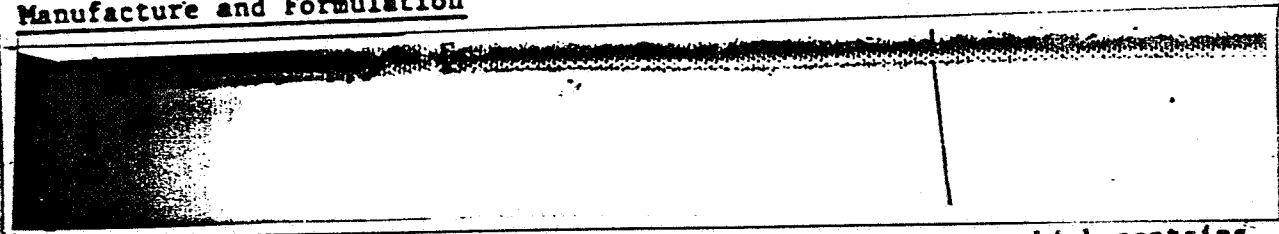
We recommend against the proposed tolerance for the reason cited in Conclusions 3c and 4a.

There are no Canadian or Mexican tolerances for glyphosate on cottonseed or meat and milk, and no Codex proposals for glyphosate.

We defer to TOX for their determination of the necessity of obtaining the information regarding [] content of the formulated product which was requested 12/4/80 (memo of 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, [] 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 [], but the name of the surfactant and the level of [] were not given. [] 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 product (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, PHS to DAA,

MANUFACTURING / INERT INGREDIENT INFORMATION DELETED

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). 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 0.75 - 3.75 lb a.i./A in 20 to 60 gal/A by ground equipment or 5 to 15 gal/A aerially. Add 0.5% (by volume) approved nonionic surfactant if desired.

Apply to cotton after 80% of bolls are opened. Do not feed or graze treated areas within 8 weeks after application. Do not apply to crops grown for seed. There is a 7 day PHI.

Currently registered uses of glyphosate on cotton are a pre-plant use of 0.75 - 3.75 lb a.i./A and a recirculating sprayer treatment using 3 lb a.i./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.

The recirculating sprayer system differs from the currently proposed use in that only weeds higher than the cotton plant are intentionally contacted by the spray foliar contact with the cotton plant is incidental—thus residue levels are lower than those expected from foliar spray.

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. 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 purpose 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.

Adequate analytical methodology is available to enforce the proposed tolerance.

Residue Data

Twelve residue studies reflecting topical application of glyphosate to cotton were submitted in PP#1G2440; 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 recovery.

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 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 ppm 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 J. Richardson, Monsanto to R. Quick, RCB on 2/13/81).

The requested tolerance level of 15.0 ppm appears adequate to cover residues of glyphosate and its metabolite, aminomethylphosphonic acid, which are likely to result from the proposed use (including already registered uses of Roundup).

Residue levels in cotton hay are reported for the same studies (0 to 14 day PHI). 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 aminomethylphosphonic acid were 0.12-0.38 ppm. Levels of N-nitrosoglyphosate were not reported.

Statistical analysis of the cotton hay residue data indicates that the half life of glyphosate in cotton hay is ca. 1 week. We therefore conclude that combined residues of glyphosate and aminomethylphosphonic acid in cotton hay would not be expected to exceed 15 ppm at the proposed 8 week interval, the same level as is established for soybean, forage and hay. Cotton forage would appropriately be included at this level.

No tolerance for cotton hay is requested, although residue data are available. Either a total restriction against feeding cotton forage and hay or a tolerance proposal for cotton forage and hay will be necessary. The proposed 8 week restriction against feeding or grazing treated against feeding treated cotton plants. A 15 ppm level would be appropriate for a tolerance. Either revised Section F (tolerance proposal) or a revised Section B (complete grazing restriction) should be submitted.

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). We therefore conclude that no food additive tolerances are necessary.

Meat, Milk, Poultry and Eggs

Cottonseed may comprise up to 25% of the diet of beef cattle and 20% for dairy cattle; cotton forage and hay may be comprise up to 20% for beef cattle and 40% for dairy cattle. 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 maximum dietary intake for 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. Residues were not detectable (<0.05 ppm) at the 100 ppm feeding level in muscle, fat or milk. In swine kidney, residues of glyphosate were 0.11 ppm at the 10 ppm feeding level and 0.42 ppm at the 30 ppm feeding level and 0.93 ppm at the 100 ppm feeding level; metabolite residues were ND (<0.05 ppm) at the 10 and 30 ppm feeding levels and 0.20 ppm at the 100 ppm level. In cattle kidney, the 10 ppm level was not analyzed. The 30 ppm level gave 0.67 ppm parent and 0.13 ppm metabolite, and the 100 ppm level gave 1.18 ppm parent and 0.46 ppm metabolite. Liver residues were lower in both swine and cattle.

The established liver and kidney tolerances of 0.1 ppm are not adequate to cover residues resulting from the increased levels in the diet due to the requested increase in the tolerance level for cottonseed. A tolerance of 0.5 ppm for the liver and kidney of cattle, goats, hogs, horses, poultry and sheep would be more appropriate. A revised Section F should be submitted.

Since no detectable residues were found in meat, fat, meat byproducts (except liver and kidney), milk or eggs at feeding levels of 100 ppm, the proposed use would fall into Category 3 of Section 180.6(a) with respect to secondary residues in these commodities.

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

TS-769:Reviewer:LMB:LDT:X77324:CM#:2:RM:810:Date:2/18/81
RDI:Section Head:RJH:Date:2/12/81:RDS:Date:2/18/81

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	0.00537
Root Crop Veg(133)	0.200	11.1	0.00222
Tree & Poa 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 3.0000 mg/day (60kg) TMRC 0.2163 mg/day (1.5kg) % ADI 7.21

Unpublished, Tox Approved PP# 8E2122, 9H5196, 9F2163, 9H5204, 0F2329, 0E2421

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
Cranberries(44)	0.200	0.03	0.00009

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

Current Action PP# 1G2240

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Glyphosate

PETITION NO 1F2455

CCPR NO. _____

Codex Status

Proposed U. S. Tolerances

No Codex Proposal
Step 6 or above

Residue (if Step 3): _____

None

Residue: N-phosphono methylglycine
and aminomethyl phosphonic acid

Crop(s) Limit (mg/kg)

Crop(s) Tol. (ppm)

None on these
commodities

cottonseed 15 ppm
cottonseed hay
liver
kidney

CANADIAN LIMIT

MEXICAN TOLERANCIA

Residue: N-(phosphono-
methyl glycine)

Residue: None

Crop Limit (ppm)

Crop Tolerancia (ppm)

None on these
commodities

None

Notes:

File last updated 3/5/81

ACCEPTABLE DAILY INTAKE DATA

RAT, Older NOEL	S.F.	ADI	HPI
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)
Cottonseed (41)	6.000	0.15	0.01350
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
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
Some 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

HPI 3.0000 mg/day (60kg) TMRC 0.2163 mg/day (1.5kg) & ADI 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
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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
Cranberries (44)	0.200	0.03	0.00009
Guava (184)	0.200	0.03	0.00009
Papayas (109)	0.200	0.03	0.00009

HPI 3.0000 mg/day (60kg) TMRC 0.5716 mg/day (1.5kg) & ADI 19.05
