

US EPA ARCHIVE DOCUMENT



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

DATE: October 29, 1981

SUBJECT: PP#1F2518 Glyphosate on forage grasses and forage legumes. Evaluation of analytical method and residue data.

FROM: Karl H. Arne, Ph.D, Chemist *K.H. Arne*
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

TO: Robert J. Taylor, Product Manager #25
Fungicide-Herbicide Branch
Registration Division (TS-767)

and

Toxicology Branch ✓
Hazard Evaluation Division (TS-769)

THRU: Charles L. Trichilo, Branch Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

Monsanto Agricultural Products Co. proposes tolerances for the combined residues of the herbicide glyphosate and its metabolite aminomethylphosphonic acid (AMP) on forage grasses at 5.0 ppm and forage legumes at 30 ppm.

Tolerances for Glyphosate are established for several RAC's ranging from 0.1 ppm for the liver and kidneys of cattle, goats, hogs, sheep, horses and poultry to 15 ppm for soybean forage and hay (Section 180.364). Tolerances are pending for several commodities including 0.2 ppm for forage grasses and 0.4 ppm for forage legumes.

Conclusions

1. The nature of the residue is adequately understood. In both plants and animals the residue of concern consists of the parent and a metabolite, aminomethylphosphonic acid.
2. Adequate analytical techniques are available for enforcement of the proposed tolerances.

3. The petitioner proposes tolerances for forage grasses and forage legumes (except peanuts). However, 40 CFR 180.34(f) allows these crop group tolerances only if residues are expected to be negligible. Since relatively high residues will result from this use, tolerances will be needed for each commodity. The petitioner should submit a revised Section F in which appropriate tolerances (see conclusion 8) are proposed for pasture grasses and for the individual legumes on which use is intended.
4. The proposed label would reduce the 8 week post application grazing restriction (now in effect for several crops) to 7 days. A revision such as this that affects crops other than the subject crops is outside the realm of this petition. The 8 week grazing restriction should remain on the label for the crops already registered. A second grazing restriction should be imposed for the subject crops.
5. The label proposes use for forage grasses and forage legumes. The petitioner should submit a Revised Section B in which use is proposed for the RAC's for which tolerances are proposed (see conclusion 3).
6. We consider grazing and feeding restrictions to be practical for fields and pastures (where livestock can be removed from the treated area) but not for rangeland as livestock are commonly left on rangeland, even as the pesticide is being applied. We therefore require a label restriction excluding this use from rangeland. The label should also include a restriction prohibiting use when livestock are present.
7. The label restriction limiting spot treatments to 10% of the total acreage is somewhat indefinite as it does not establish a maximum size for a "spot". We suggest the following restriction. "Spot treatments should not exceed 1/10 of an acre in size. No more than 10% of any given acre may be treated."
8. The data do not support the proposed tolerances. The maximum residues at the proposed 7 day grazing restriction interval are: for forage grasses, 153 ppm; for forage legumes, 162 ppm. If the petitioner imposes (or revises) the label restrictions as suggested in conclusions 4,5,6 and 7 we would recommend for tolerances of 200 ppm. The petitioner should propose tolerances of 200 ppm for pasture grass and for those legumes for which use is intended. The tolerance should include their respective hays.

9. For the purposes of determining secondary residues in meat and milk we will assume that treated crops will account for no more than 10% of the pasture grasses or forage legumes ingested by livestock. Thus, feeding the subject crops to livestock would add 20 ppm, not 200 ppm to the diet.

Based on cattle feeding studies at 10, 30 and 100 ppm in the diet we conclude that tolerances of 0.5 ppm are needed for the liver and kidney of cattle, horses, goats, hogs and sheep. There is no reasonable expectation of residues in the meat fat and meat by-products (other than liver and kidney) of cattle, horses, hogs, sheep and goats or in milk.

10. Existing tolerances will accommodate residues in the liver and kidneys of poultry. There is no reasonable expectation of secondary residues in eggs and in the meat, fat and meat byproducts of poultry (other than liver and kidney).
11. An International Residue Limit Status sheet is attached. There are no Codex proposals for glyphosate. The Canadian Limit for glyphosate (only the parent compound is regulated) on forage grasses and forage legumes is 0.1 ppm (negligible).

Recommendation

We recommend against the proposed tolerance. For a favorable recommendation we require the following:

1. The petitioner should submit a revised Section B in which the following revisions and/or additions are included.
 - a. A 7 day post application grazing and feeding restriction should be imposed for the subject crops only. The more general 8 weeks grazing and feeding restriction should remain on the label.
 - b. Use should be proposed for pasture grasses and for those legumes for which use is intended.
 - c. A label restriction excluding this use from rangeland should be imposed.
 - d. A label restriction prohibiting application when livestock are present should be imposed.
 - e. The following label restriction should be imposed:
"Spot treatments should not exceed 1/10 of an acre in size. No more than 10% of any given acre should be treated."

2. The petitioner should proposed tolerances for pasture grasses and for those legumes for which use is intended, all at 200 ppm. The tolerance should include their respective hays.
3. Tolerances of 0.5 ppm should be proposed for the liver and kidney of cattle, horses, sheep, hogs and goats.

Detailed Considerations

Manufacture and formulation

The manufacturing process for technical glyphosate has been previously submitted and reviewed. (e.g., PP#6G1826, memo of 11/30/76, D. Duffy).

Roundup, the formulation proposed for use, is an aqueous concentrate containing 41% (4 lbs/gallon) isopropylamine salt of glyphosate. This is equivalent to 3 lbs glyphosate per gallon.

The inert ingredients in this formulation consist of the (cleared under 40 CFR 180.1001

(d)),

which are not expected to present a residue problem.

An additional impurity in the formulated product (an impurity in the technical material as well) is N-nitrosoglyphosate (NNG) which has been reported to be in Roundup at levels of 0.2-0.4 ppm. NNG has been subjected to a hazard assessment review (see 8/24/78 memo of R. Taylor, FUS to OPP, EPA) with the result that OPP does not bar the establishment of glyphosate tolerances because of this impurity.

Proposed Use

For control of a annual and perennial weeds in forage grasses and forage legumes Roundup is to be applied as a spot treatment at rates of up to 3.75 lb a.i./A. The combined total of all treatments must not exceed 6 lb a.i./A/year. Treated areas are not to be grazed within 7 days of the last treatment. There is to be a 28 day PHI for hay. No more than 10% of the total acreage is to be treated.

We suggest the label be revised as follows:

1. The label should specify the crops to be treated, not simply forage grasses and forage legumes. That is, use should be proposed for pasture grasses and for those legumes for which use is intended.

INERT INGREDIENT INFORMATION DELETED

2. The label proposed would reduce the 8 week grazing and feeding restriction (now in effect for several crops) to 7 days. The shorter interval may be acceptable for forage grasses and forage legumes but a revision that affects crops other than the subject crops is outside the realm of this petition. The 8 week grazing and feeding restriction should remain on the label; a separate grazing and feeding restriction (7 days) should be imposed for pasture grasses and for those legumes for which use is intended.
3. We consider a 7 day grazing and feeding restriction to be practical for fields and pastures (where livestock can be removed from the treated area) but not for rangeland as livestock (except dairy) are commonly left on rangeland even as pesticides are being applied. We therefore require a label restriction excluding this use from rangeland. We also require a label restriction prohibiting application when livestock are present.
4. The restriction limiting this use to no more than 10% of the total acreage is somewhat indefinite as it places no limit on the size of a "spot". We suggest the following: "Do not treat areas larger than 1/10 of an acre. No more than 10% of any given acre may be treated". We consider this restriction practical because as if larger areas were treated they would need to be reseeded; this costs money, time and requires that livestock are removed from the area being reseeded.

Nature of the Residue

Radiotracer plant metabolism studies (corn, soybeans, wheat, cotton, rice, barley, oats, sorghum, sugarbeets, sugarcane, potatoes, vegetable crops, grapes, coffee and citrus orchard fruits) have been submitted in conjunction with several petitions and were discussed in our reviews.

In all cases the major degradative pathway of glyphosate has been shown to entail C-N bond cleavage to form glyoxylate and the major metabolite, aminomethylphosphonic acid (AMP). Further metabolism involves significant incorporation of fragments of these compounds into natural plant products.

Tracer studies (submitted with previous petitions) in rats, rabbits and cows indicate that most of the radioactive dose is excreted (90% within 5-7 days) primarily in the feces. The major component of the residue is the parent with only trace amounts of AMP being found.

We conclude that the metabolism of glyphosate in plants and animals is adequately understood.

Analytical Method

The method used to gather residue data is very similar to the method that has been successfully tried out on soybeans. Parent and metabolite are determined as separate entities.

Briefly, the sample is ground (while frozen) then extracted with deionized water. The sample is filtered; the filtrate is column chromatographed on Al010 resin. Glyphosate and aminomethylphosphonic acid are eluted with 0.5M ammonium carbonate. The resulting solution is treated with charcoal. The charcoal is removed and the water is evaporated using a rotary film evaporator.

The two compounds are then separated by column chromatography on AG50W-X8. Precise directions for elution are followed to assure cleanly separated fractions. Both compounds are converted to their N-trifluoroacetylmethyl derivatives then determined by GLC using a phosphorus specific flame photometric detector.

The following recovery values are presented.

<u>crop</u>	<u>recovery (glyphosate)</u>			<u>recovery (AMP)</u>		
	<u>fort.(ppm)</u>	<u>range (%)</u>	<u>avg.</u>	<u>fort.</u>	<u>range (%)</u>	<u>avg.</u>
legumes	0.05-40	50-118	73	0.05-40	48-105	73
grasses	0.05-40	41-111	66	0.05-40	43-113	67

Glyphosate check values were <0.05 ppm for legumes and <0.05-0.06 ppm for grasses. All check values for AMP were <0.05 ppm.

An HPLC method has also undergone a successful method trial (see PP#0F2329, memo of 1/19/81, R.W. Storherr) and is suitable for confirmatory analysis.

Satisfactory methods are available for enforcement purposes.

Residue Data

Several types of forage grasses and forage legumes were spot treated with 4.5 lb a.i./A Roundup (the proposed max. rate is 3.75 lb a.i./A). Samples for residue analysis were taken from the treated area, the area just outside the treated area that was affected by glyphosate (e.g., by drift) and from the unaffected area to a distance ca. 100 ft from the affected area.

The following residue data are from the treated area:

Grasses

<u>State</u>	<u>variety</u>	<u>PHI</u>	<u>Glyphosate*</u>	<u>AMP*</u>	<u>total**</u>
IN	fescue	7	21	0.24	18
		28	3.4	0.16	3.0
DE	orchardgrass	7	174	6.4	153
	bluegrass				
GA	bahiagrass	7	4.8	2.6	6.2
	bromegrass	28	0.6	1.3	1.6
	ceresia lespodeza				
NM	Kentucky	7	5.7	2.1	6.4
	bluegrass	28	1.8	1.6	2.8
TX	calli bermuda	7	2.1	4.1	5.2
		28	5.2	1.7	5.8

Legumes

CA	alfalfa	7	78	0.1	65
		14	47	2.0	41
		28	95+	3.9+	83+
		60	19	0.6	16
NY	alfalfa	7	5.1	1.2	5.2
		28	1.6	1.1	2.2
WI	alfalfa	7	191	4.4	162
		28	58	1.3	50
NY	birdsfoot	7	49	0.6	41
	trefoil	28	1.0	<0.05	0.83
NC	ceresia	7	70	4.9	63
	lespodeza	28	5.9	1.0	57

+ we consider these values to be anomolous

* in ppm corrected for recovery.

** corrected for both recovery and for the exaggerated rate used in the tests.

As would be expected, relatively little residue was found in the untreated areas. The affected area (just outside the treated area) was found to have, at maximum, residues of 4.1 ppm for grasses and 22 ppm for legumes when sampled 7 days after treated. Samples from the unaffected area carried residues that were, for the most part, at or near the limit of detectability (0.05 ppm for either compound).

Conclusions

The petitioner has proposed group tolerances for forage grasses and forage legumes. However 40 CFR 180.34(f) allows these group tolerances only if residues are expected to be negligible. Since relatively high residues will result from the proposed use tolerances will be needed for each commodity. Therefore the petitioner should propose appropriate tolerances (see below) for pasture grasses and for those legumes for which use is intended.

Based on the submitted data we conclude that tolerances of 200 ppm are needed for pasture grasses and for those legumes for which use is intended. This level will also accommodate expected residues in hay harvested 28 days after application.

Meat and Milk

For the purposes of establishing meat and milk tolerances we will assume that the treated crop will consist of no more than 10% of the pasture grasses or legumes ingested by livestock. That is, for feeding purposes we will consider the forage grasses and legumes to bear residues of 20 ppm.

We calculate that the proposed use could add 16 ppm to the diet of cattle as follows:

200 ppm tolerance x 10% of crop that may be treated x 80%
maximum diet = 16 ppm

Feeding studies have been conducted on lactating cows (PP#5F1536) at 10, 30 and 100 ppm. No residue was found in milk, muscle or fat at any level. Residues in kidneys and liver (at the 100 ppm level) were as high as 1.64 ppm. From these results we conclude that a tolerance of 0.5 ppm is needed for the liver and kidneys of cattle. We extend this conclusion to include the liver and kidneys of horses, hogs, goats and sheep. We conclude that there is no reasonable expectation of residues on the meat, fat, meat byproducts (other than liver and kidney) and milk of these livestock.

Poultry and Eggs

Poultry are not normally fed grasses. Alfalfa meal may comprise 5% of their diet; seeds and screenings, 20%. If treated alfalfa seeds and screenings were fed to poultry it could add up to 4 ppm glyphosate residues to the diet (200 ppm x 10% of crop that may be treated X 20% in diet).

No residues were found in the eggs, fat or meat of chickens fed glyphosate at levels of up to 100 ppm. Residues of up to 0.10 ppm were found in the liver of chickens fed 100 ppm glyphosate. Based on these studies we conclude that the existing tolerances for the liver and kidneys of poultry (0.2 ppm) is adequate and that there is no reasonable expectation of residues in eggs or in the meat fat and meat byproducts (other than kidneys and liver) of poultry.

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

TS-769: Reviewer: K. Arne: LDT: X77324: CM#2: RM: 810: Date: 9/20/81
RDI: Section Head: RSQ: Date: 9/19/81: RDS: Date: 9/19/81

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Glyphosate

PETITION NO. 1E2518 (K. Arne)

CCPR NO. _____

Codex Status

Proposed U.S. Tolerances

No Codex Proposal Step
6 or above

Residue (if Step 9): _____

Residue: 1) N-phosphonomethylglycine

2) aminomethylphosphonic acid

Crop(s) Limit (mg/kg)

Crop(s) Tol. (ppm)

There are no Codex proposals for
this chemical.

forage grasses 30.0
forage legumes 5.0

CANADIAN LIMIT

MEXICAN TOLERANCIA

Residue: _____

Residue: _____

Crop Limit (ppm)
grasses 0.1 (negligible)
forage legumes 0.1 (negligible)

Crop Tolerancia (ppm)
None

Notes: