(2C)

MAR 3 1981

Memorandum

SUBJECT: PP#0F2421. Glyphosate on cranberries. Evaluation of analytical method and residue data.

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TO: C. Fletcher, Product Manager No. 43
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THRU: Charles L. Trichilo, Chief
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Hazard Evaluation Division (TS-769)

Monsanto Agricultural Products Co. and Dr. N. F. Kupelian, IR-4 National Director, on behalf of the IR-4 Technical Committee and the Agricultural Experiment Stations of Massachusetts, New Jersey, Washington and Wisconsin propose a tolerance of 0.2 ppm for the combined residues of glyphosate (Roundup®, N-phosphonomethylglycine) and its metabolite, aminomethylphosphonic acid on cranberries.

Tolerances for residues of glyphosate (which include the parent and aminomethylphosphonic acid, a metabolite) are established for several RAC's ranging from 0.1 ppm for the liver and kidneys of cattle, goats, horses, hogs, sheep and poultry to 15 ppm for soybean forage and hay (Sec. 180.364).

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. N-nitrosoglyphosate (NNG) is an impurity in the formulated product. The presence of NNG in the formulated material has been subjected to a hazard assessment review with the result that OPP does not bar the establishment of glyphosate tolerances because of the presence of this impurity.

3. Adequate analytical techniques are available for enforcement of the proposed tolerance.

4. From the proposed winter application we expect no detectable residues of the parent or aminomethylphosphonic acid (<0.05 ppm each) in cranberries. The proposed tolerance is adequate.

5. Since no food items are involved there will be no problem of secondary residues in meat, milk, poultry and eggs.

6. [illegible] has recently expressed concern over the level of [redacted] as an impurity in a surfactant inert ingredient in the formulation. Little, if any, residue of [redacted] would be expected in cranberries from the proposed use.

7. We are uncertain as to how much, if any, glyphosate residues might be present in the water from flooded cranberry bogs at harvest and therefore require a label restriction that prohibits the use of this water for irrigation of other crops. If this restriction is unacceptable to the petitioner we will require analyses of flood water from treated bogs.

8. An International Residue Limit Status Sheet is attached. No tolerances for glyphosate on cranberries are established outside the United States.

INERT INGREDIENT INFORMATION DELETED

Recommendations:

Toxicological and [illegible] considerations permitting, and provided a label restriction prohibiting the use of harvest flood water for irrigation of other crops is imposed, we recommend for the proposed tolerance.

DETAILED CONSIDERATIONS

The manufacturing process for technical glyphosate has previously been submitted ([illegible]) and detailed in our reviews (e.g., [illegible] Duffy, memo of 11/30/76, [illegible]).

The technical product is formulated as an aqueous concentrate containing 41% of the isopropylamine salt of glyphosate. This formulation, tradename Roundup®, contains 4 lbs of the isopropylamine salt per gallon which is equivalent to 3 lbs of glyphosate per gallon.

[redacted]

An additional impurity in the formulated product (an impurity in the technical material as well) is N-nitrosoglyphosate ([illegible]) which has been reported to be in Roundup at levels of [illegible] ppm. [illegible] has been subjected to a hazard assessment review (see [illegible]/24/77 memo of R. Taylor, [illegible] to [illegible], [illegible]) with the result that [illegible] does not bar the establishment of glyphosate tolerances because of the presence of this impurity (as per R. Taylor memo [illegible]/5/78).

[redacted] is present as an impurity in a surfactant used in Roundup. [illegible] has withheld their support from recent petitions ([illegible] 1[illegible]244) and 1[illegible]244, glyphosate on quavas and papayas, respectively, memo of 2/[illegible], [illegible] until questions raised about this impurity can be resolved. Little, if any, [redacted] residue would be expected on cranberries from the proposed use. [redacted] is cleared for use as a solvent under [illegible] [illegible].1001(4).

5. Since no feed items are fortified there will be no problem of secondary residues in meat, milk, poultry and eggs.

6. TOX has recently expressed concern over the level of [redacted] as an impurity in a surfactant inert ingredient in the formulation. Little, if any, residue of [redacted] would be expected in cranberries from the proposed use.

7. We are uncertain as to how much, if any, glyphosate residues might be present in the water from flooded cranberry bogs at harvest and therefore require a label restriction that prohibits the use of this water for irrigation of other crops. If this restriction is unacceptable to the petitioner we will require analyses of flood water from treated bogs.

8. An International Residue Limit Status Sheet is attached. No tolerances for glyphosate on cranberries are established outside the United States.

Recommendation:

Toxicological and EFS considerations permitting, and provided a label restriction prohibiting the use of harvest flood water for irrigation of other crops is imposed, we recommend for the proposed tolerance.

DETAILED CONSIDERATIONS

The manufacturing process for technical glyphosate has previously been submitted (PP#4F1809) and detailed in our reviews (e.g., D. Duffy, memo of 11/30/76, PP#6G1826).

The technical product is formulated as an aqueous concentrate containing 41% of the isopropylamine salt of glyphosate. This formulation, tradename Roundup®, contains 4 lbs of the isopropylamine salt per gallon which is equivalent to 3 lbs of glyphosate per gallon.

manufacturing information deleted

[redacted]

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, FDS to DAA, CPP) with the result that CPP does not bar the establishment of glyphosate tolerances because of the presence of this impurity (as per R. Taylor memo 9/5/78).

[redacted] is present as an impurity in a surfactant used in Roundup. TOX has withheld their support from recent petitions (PP#s 1E2443 and 1E2444, glyphosate on guavas and papayas, respectively, memo of 2/5/81, W. Dykstra) until questions raised about this impurity can be resolved. Little, if any, [redacted] residue would be expected on cranberries from the proposed use. [redacted] is cleared for use as a solvent under 40 CFR 180.1001(d).

Proposed Use:

For control of weeds in cranberry bogs glyphosate is to be applied with a wiper applicator. A wiper applicator is either a roller or wick device which carries the herbicide in an absorbent material; application is made by wiping the material directly on the weeds. Since cranberry vines do not reach a height of more than several inches the wiper application will selectively contact weeds. Care is to be taken to avoid contact of glyphosate with desirable vegetation. For maximum effectiveness two applications, one from either direction, are suggested. The rate of application varies with the severity of infestation; the highest rate is 5 qts. Roundup (3.6 lb. glyphosate)/A applied as a 20% solution of the formulation (8% a.i.). Repeat applications may be necessary but no more than 8 qts of Roundup (6 lbs glyphosate may be applied per year. Application is to be made after fruit set but no later than 30 days before harvest.

Nature of the Residue:

Radiotracer plant metabolism studies (corn, soybeans, wheat, cotton, rice, barley oats, sorghum, sugarbeets, sugarcane, potatoes, vegetable crops, grapes, coffee a citrus orchard fruits) have been submitted in conjunction with several glyphosate 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, aminomethylphosph acid (CP 50435). Further metabolism involves significant incorporation of fragm of these compounds into natural plant products.

(From the proposed use there is no application of Roundup to cranberries, only to the weeds above the crop; any residue in the fruit would be expected to be contaminative in nature.)

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

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

Analytical Methods:

The method used to gather residue data for cranberries is very similar to that used for enforcement. Glyphosate and its major metabolite, aminomethylphosphon acid, are determined separately.

Briefly, a plant sample is extracted (in a blender) with water-chloroform. The aqueous phase, which contains both compounds, is cleaned up with charcoal, then with an ion exchange column. The two compounds are separated by column chromat on AG 50-X8. Precise directions for elution (with deionized water) are followe obtain cleanly separated fractions. Trifluoroacetic anhydride is used to conve both compounds to the N-trifluoroacetylmethyl ester derivatives which are than determined by GLC using a phosphorus specific flame photometric detector.

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Cranberries fortified with 0.05-0.3 ppm glyphosate gave recoveries of 47-94% (avg 66%); fortified with 0.05-0.3 ppm aminomethylphosphonic acid the recovery ranged from 55 to 71% (avg. 68%). Check values were <0.05 ppm for glyphosate and <0.01 ppm for aminomethylphosphonic acid.

A successful HPLC Method tryout for glyphosate in peanuts has recently been completed (PP#OE2329, memo of 1/19/81, R.W. Storherr). Earlier a similar method had been successfully tried out on tomatoes and cottonseed (memo of 9/19/80, R.W. Storherr). The HPLC method is less time consuming but not as sensitive as the method used to gather data for cranberries and is suitable for confirmatory analysis.

We conclude that adequate analytical techniques are available for enforcement purposes.

Residue Data:

Residue experiments were carried out in New Jersey, Washington, Massachusetts and Wisconsin. The only significant cranberry producing state unrepresented in these experiments is Oregon.

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One or two applications of the maximum proposed rate (20% Round-up, equivalent to 8% glyphosate) resulted in no detectable residue in the cranberries at PHI's ranging from 29 to 84 days.

We conclude that residues of glyphosate in cranberries as a result of the proposed use will not exceed the proposed tolerance.

Meat, Milk, Poultry and Eggs:

Since no livestock or poultry feed items are involved there will be no problem of secondary residues in meat, milk, poultry and eggs.

Tolerances (p

Other Considerations:

Where cranberries are wet harvested the bogs would be flooded at least 30 days after application of glyphosate. We do not expect that significant concentrations of glyphosate residues would occur in this water but since no data are available w can draw no conclusions. Therefore we require a label restriction that prohibits the use of harvest flood water from treated bogs for irrigation of other crops.

TS-769:RCB:K. Arne:gs:X77324:CM#2:RM810:2/26/81
cc:RF., CIRC., ARNE, FDA, WATTS, TOX, EEB, EFB, PP#OE2421
RDI: Quick, 2/26/81:Schmitt, 2/26/81

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Glyphosate(N-(phosphonomethyl)-glycine

PETITION NO. OF2421 (Arne)

CCPR NO. —

Codex Status

[X] No Codex Proposal
Step 6 or above

Residue (if Step 9): NONE

Crop(s)	Limit (mg/kg)
NONE	

Proposed U.S. Tolerances

N-(phosphonomethyl)glycine and aminomethylphosphonic acid

Residue:

Crop(s)	Tol. (ppm)
Cranberries	0.2

CANADIAN LIMIT

Residue: N-(phosphonomethyl)glycine

Crop	Limit (ppm)
NONE ON THIS COMMODITY	

MEXICAN TOLERANCIA

Residue: NONE

Crop	Tolerancia (p
NONE	

NOTES:

CFR 180.364 Glyphosate Roundup 4/8/80

File last updated 4/8/80

ACCEPTABLE DAILY INTAKE DATA

RAT, Older NOEL mg/kg	NOEL ppm	S.F.	ADI mg/kg/day	MPI 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

MPI	TMRC	% ADI
3.0000 mg/day/60kg	0.2078 mg/day/1.5kg	6.93

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Unpublished,Tox Approved 8E2122,9H5196,9F2223,9F2162

CROP	Tolerance	Food Factor	mg/day/1.5kg
Sugar,cane&beet(154)	1.500	3.64	0.10369
Molasses(96)	18.000	0.03	0.00828
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	0.3279 mg/day/1.5kg	10.93

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Current Action P29F2163,9H5204,0F2329

CROP	Tolerance	Food Factor	mg/day/1.5kg
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
[illegible]	0.100	133.33	0.20000

NPI	THRC	% ADI
3.0000 mg/day/ :g	0.5709 mg/day/1.5kg	19.03

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