UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: July 17, 1979

SUBJECT: PP#8E2122, PP#9H5196 Tolerance request for glyphosate in or on sugarcane at 2.0 ppm and food additive tolerance request for glyphosate in or on molasses at 20.0 ppm and raw sugar at 2.0 ppm. Acc.#097402, EPA Reg.#524-Mon-8000, CASWELL#661A

FROM: William Dykstra, Ph.D
Toxicology Branch (TS-769)

WDD 7/17/79

TO: Robert Taylor & RCB, TS-769
Product Manager#25

Petitioner: Monsanto Agricultural Products, Inc.
800 N. Lindbergh Boulevard
St. Louis, Mo. 63166

Recommendations:

1. The registration can be toxicologically supported.

2. The recommendations of the "Free Standing" summary of PP#8E2122 and PP#9H5196 are contained herein.

Proposed Tolerances

A request is made to establish a pesticide tolerance of 2 parts per million for the combined residues of N-phosphonomethylglycine (glyphosate) and its metabolite aminomethylphosphonic acid in or on the commodity sugarcane resulting from the preharvest application of the sodium sesqui salt of glyphosate as a growth regulator.

Sugarcane ---------- 2.0 ppm

Tolerances have been established to adequately cover residues that would result in the liver and kidney of cattle, goats, hogs, horses, poultry and sheep from the proposed uses as delineated in 180.6 (a) (2) and there is no reasonable expectation of finite residues resulting in other meat products, eggs or milk as delinated in 180.6 (a) (2).

Residues actually seen in sugarcane at 7 locations were all less than the proposed 2.0 ppm proposed tolerance where MON 8000 (sodium salt of glyphosate) was applied at the maximum projected use rate of 1.0 lb/A. a.e. (1.6 lb product/A) and sampled at the minimum 10 day treatment to harvest interval.

A FOOD ADDITIVE TOLERANCE is also requested for the combined residues of N-phosphonomethylglycine (glyphosate) and its metabolites, aminomethylphosphonic acid when present therein as a result of the application of the sodium sesqui salt of glyphosate as a plant growth regulator as follows:

Molasses ---------- 20.0 ppm

Raw Sugar ---------- 2.0 ppm

Molasses requires a food additive tolerance since glyphosate can concentrate in this processed mill fraction when MON 8000 is applied pre-harvest to sugarcane as a cane ripening agent. The actual residues detected in molasses were less than the proposed 20.0 ppm tolerance.

A FOOD ADDITIVE TOLERANCE is requested for raw sugar both because it is at the same level as sugarcane and also to cover any residues found in this commodity when it is imported.

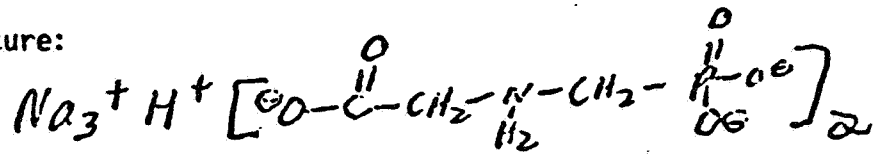
A. Substance Identification

1. Chemical Name: Sodium N-(phosphonomethyl) gkycine

2. Synonyms: MON-8000, Roundup, glyphosate

3. Purity of technical material: 98% pure

4. Structure:



B. Referenced Petitions: 4G1444, 5G1561, 5G1523, 5F1536, 5F1560, 6G1734, 6G1679, 6E1809, 6G1826, 6G1862, 6G1757, 6F1861, 6F1758, 6H5144, 6F1733, 7G1893, 7G1903, 7F1904, 8F2080, 8F2070

C. Formulation

MON-8000

Ingredient	Percent Weight
Sodium N-(phosphonomethylglycine)	75.0
[redacted]	[redacted]
	100.00

INERT INGREDIENT INFORMATION DELETED

Inerts cleared under 180.1001(c) and (e).

D. Uses Proposed:

Apply in 30 to 90 liters of water per Hectare. Equipment should be thoroughly flushed with water after each use to avoid possible corrosion.

Apply to 0.5 to 1 Kilogram of this product per hectare at least 3 weeks before harvest. Harvesting shoudl be concluded 8 weeks after application.

Review

1. Previously submitted Toxicology Studies

   a. Memo of 4/17/78 from W. Dykstra to L. Welch.

   b. Memo of 8/22/78 from R. Engler to R. Taylor. TOX Branch recently reviewed the validated studies in support of the pesticide glyphosate.

1. Data Considered:

Oral LD50 rabbit: 3.8 gm/kg (valid)
90-day Rat Feeding: NOEL = 2000 ppm (valid)
90-day Dog Feeding: NOEL = 2000 ppm (valid
Teratology (2 studies) rabbit: NOEL = 30 mg/kg/day (highest dose) (repeat studies with higher do
2-year Dog Feeding: NOEL = 300 ppm (valid)
3-generation Rat Reproduction: NOEL = 100 ppm (valid)
18-month Mouse Feeding: No carcinogenic potential at 300 ppm (highes dose). Study must be repeated since too man animals are missing.
2-year Rat Feeding: NOEL = 100 ppm (valid). Study is adequate to determine toxic effects but only marginal with respect to oncogenic evaluation since too few animals examined. As reported study shows no oncogenic potential.
Neurotoxicity (hen): negative 7.5 gm/kg (cumulative for 3 days) (val

Mutagenicity Tests:

(i) dominant lethal (mice): negative at 10 mg/kg (highest dose), supplemental study, no records of posit controls.

(ii) host-mediate assay: negative (valid)

(iii) Ames test: negative (supplemental study) no raw data availabl

(iv) Rec-Assay: negative (supplemental study), no raw data availabl

2. No new toxicity data were submitted with this petition.

3. Evaluation of ADI.

The ADI is based on the NOEL of 100 ppm (5 mg/kg/day) in a 2-year rat feeding study. This is the most sensitive species for which chronic data are available. A 100 fold safety factor was used to calculate t ADI.

$$ADI = NOEL \times \frac{1}{100}$$

$$ADI = 5 \text{ mg/kg/day} \times \frac{1}{100} = 0.05 \text{ mg/kg/day}$$

The MPI for a 60 kg person is 3 mg/day

5. Tolerances have been established under 40 CFR 180.364.

6. The published tolerances utilize 6.93% of the ADI. An unpublished tox approved tolerance utilizes the ADI to 7.05%. The current action utilizes the ADI to 10.78%. Therefore the current action utlizes 3.73% of the ADI (computer printout attached). Other pending tolerances utilize the ADI to 14.38%.

7. No regualtory actions are pending against the pesticide and no RPAR criteria have been exceeded.

Conclusions and Recommendations

The requested tolerance for glyphosate and the registration can be toxicologically supported. One of the main deficiencies in the glyphosate data base is the lack of an adequate teratology study.

It is however concluded that the studies at hand together with the reproduction study show that glyphosate has low potential for showing any teratologic effects. The oncogenic potanital of glyphosate is not fully elucidated. The lifetime mouse and rat studies, however, provide adequate assurance that glyphosate has a relatively low oncogenic potential. A further assurance of low risk associated with glyphosate is found in the fact that on a theoretical basis the exposure via the diet is relatively low at present. The current action utlizes 3.73% of the ADI and a toal total of 10.78% of the ADI is utilized by all present tolerances on glyphosate.

This chemical is to be for import crops only and not for application to sugar cane in the Continental U.S.A.

TOX/HED:th:RD Initial WDYKSTRA:7-17-79

CFR 180.364 ⌒ Glyphosate Roundup ⌒ 7/16/79

File last updated 7/16/79

ACCEPTABLE DAILY INTAKE DATA

RAT,Older NOEL mg/kg	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	THRC	% ADI
3.0000 mg/day/60kg	0.2078 mg/day/1.5kg	6.93

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Unpublished,Tox Approved 9G2150

CROP	Tolerance	Food Factor	mg/day/1.5kg
Stone Fruits(151)	0.200	1.25	0.00374

MPI	THRC	% ADI
3.0000 mg/day/60kg	0.2115 mg/day/1.5kg	7.05

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Current Action 8E2122,9H5196

CROP	Tolerance	Food Factor	mg/day/1.5kg
Sugar,cane&beet(154)	1.900	3.64	0.10369
Molasses(96)	10.000	0.03	0.00828

MPI	THRC	% ADI
3.0000 mg/day/60kg	0.3235 mg/day/1.5kg	10.78

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Other Pending Tolerances 8F2070/8G2051,6G1679/6H5106,8G2060,8G2032

CROP	Tolerance	Food Factor	mg/day/1.5kg
Asparagus(5)	0.200	0.14	0.00043

Fish,shellfish(59)	0.150	1.08	0.00244
Cucurbits( )	0.050	2.84	0.00213
Fruiting Vegetables(60)	0.050	2.99	0.00225
Small Fruit,berries(146)	0.050	0.83	0.00062
Potable Water(198)	0.050	133.33	0.10000
Potatoes(127)	0.000	5.43	0.00000

IIPI	TMRC	% ADI
3.0000 mg/day/60kg	0.4314 mg/day/1.5kg	14.38

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