

US EPA ARCHIVE DOCUMENT

(11)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: November 13, 1979

SUBJECT: EPA Reg. #524-308; Glyphosate; PP#9F2162; petition proposing establishment of a tolerance for residues of glyphosate and its metabolite in the crop grouping stone fruit at 0.2 ppm. CASWELL#661A

FROM: William Dykstra
Toxicology Branch (TS-769)

WHD 11/13/79 WSW

TO: Richard Mountfort
Product Manager#25

Residue Chemistry Branch
(TS-769)

THRU: Dr. Adrian Gross, Chief
Toxicology Branch (TS-769)

William S. Gutter for Mr. Adrian Gross

Petitioner: Monsanto Agricultural Product, Inc.
800 N. Lindbergh Blvd.
St. Louis, Mo. 63166

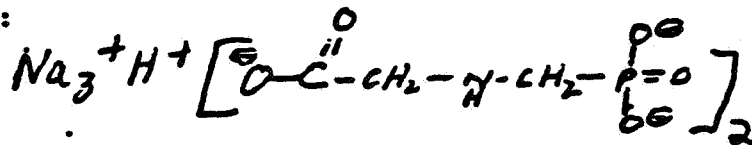
Recommendations

- 1) The requested tolerance on stone fruit can be toxicologically supported.
- 2) The recommendations of the "free-standing" summary are contained herein.

Section F - It is proposed that following an evaluation of the scientific data supplied with this request and other relevant material, that a tolerance of 0.2 ppm be established for combined residues of the herbicide glyphosate and its metabolite aminomethyl phosphonic acid in or on the raw agricultural commodities stone fruit.

A. Substance Identification

1. Chemical Name: Sodium N-(phosphonomethyl)glycine
2. Synonyms: MON-8000, Roundup, glyphosate
3. Purity of technical material: 98% pure
4. Structure:



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OK E

B. Formulation (Confidential)

Roundup

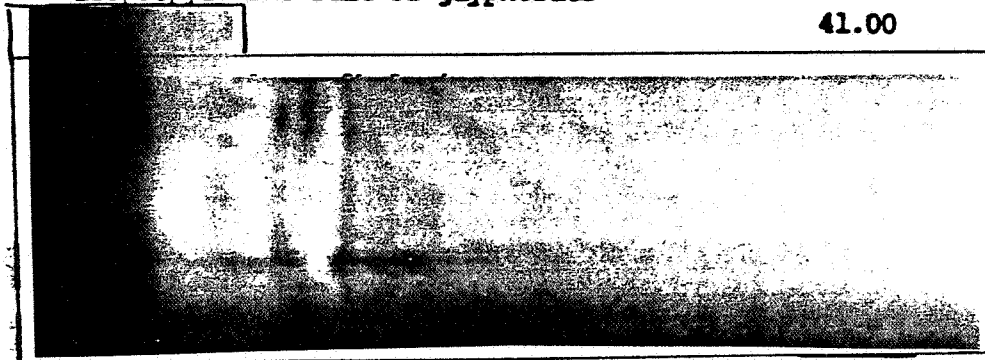
Ingredient

Percent Weight

Isopropylamine salt of glyphosate

41.00

INERT INGREDIENT
INFORMATION
DELETED



100.00

Inerts cleared under 180.1001

Review

A. Memo of 8/22/78 from R. Engler to R. Taylor. Toxicology Branch has reviewed the validated studies in support of 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)
- °Teratogenic (2 studies) Rabbit: negative at 30 mg/kg/day (highest dose); repeat studies with higher dose
- °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 (highest dose); study must be repeated since too many animals are missing.
- °2-Year Rat Feeding: NOEL = 100 ppm (valid)
Study is adequate to determine the toxic effects, but only marginal with respect to oncogenic evaluation since too few animals were examined. As reported the study shows no oncogenic potential.
- °Neurotoxicity (hen): negative at 7.5 mg/kg (cumulative for 3 days) (valid)
- °Dominant Lethal (Mice): negative at 10 mg/kg; supplemental study, no records of positive controls.
- °Host-Mediated Assay: negative (valid)
- °Ames-Test: negative (supplemental study), raw data available
- °Rec-Assay: negative (supplemental study), no raw data available.

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

(3)

3. Evaluation of the 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 toxicity data are available. A 100 fold safety factor was used to calculate the ADI.

$$\text{ADI} = 5 \text{ mg/kg/day} \times \frac{1}{10} = 0.05 \text{ mg/kg/day}$$

The MPI for a 60 kg person is 3.0 mg/day

4. Tolerances have been established under 40 CFR 180.364.
5. The published tolerances utilize 6.93% of the ADI. Unpublished, TOX approved tolerances utilize the ADI to 10.80%. The current action utilizes 0.13% of the ADI. All tolerances on glyphosate utilize 10.93% of the ADI. (Computer printout is attached).
6. No RPAR criteria have been exceeded and no regulatory actions are pending against the pesticide.

Conclusions and Recommendations

The requested tolerance for glyphosate can be toxicologically supported. One of the 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 potential of glyphosate is not fully elucidated. The life-time 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 exposure via the diet is relatively low at present.

TOX/HED:th:RD Initial WWOODROW:11-9-79

CFR 180.364

Glyphosate Roundup

11/7/79

File last updated 11/7/79

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
Pistacio 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

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

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
Bananas(7)	0.00	1.42	0.00425
Olives(104)	0.100	0.06	0.00009

MPI	TMRC	% ADI
3.0000 mg/day/60kg	0.3241 mg/day/1.5kg	10.30

Current Action 9F2162

CROP	Tolerance	Food Factor	mg/day/1.5kg
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
