

DATE: November 7, 1979

SUBJECT: EPA Reg. #524-308; Glyphosate; PP#9F2163; PP#9H5204; petitions requesting establishment of tolerances for glyphosate and its metabolite in or on the crop groupings cucurbits, fruiting vegetables, small fruits, stone fruits and the individual commodity hops at 0.1 ppm; additional tolerances are requested in shellfish and crustaceans at 2.0 ppm and for fish at 0.2 ppm; a food additive tolerance for potable water at 0.1 ppm is a part of this request. CASWELL 661A

FROM: William Dykstra
Toxicology Branch (TS-769)

WHD 11/7/79 WSW

TO: Richard Mountfort
Product Manager#25

& Residue Chemistry Branch
(TS-769)

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

Recommendations:

- 1) The requested tolerances and label amendment can be toxicologically supported.
- 2) The recommendations of the "free-standing" summary are contained herein.

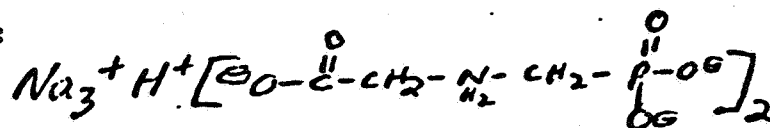
Section F - Proposed Tolerances

Tolerances are hereby requested for the combined residues of the herbicide glyphosate (N-phosphonomethyl glycine) and its metabolite aminomethylphosphonic acid, resulting from the use of irrigation water following applications on around aquatic sites, in or on the crop groupings cucurbits, fruiting vegetables, small fruits, stone fruits, and the individual commodity hops at 0.1 ppm. Where tolerances exist for these or other commodities at higher levels (CFR 180.364), the higher tolerance applies also to residues from the uses cited.

Additional tolerances are requested for shellfish and crustaceans at 2.0 ppm and for fish at 0.2 ppm. A food additive tolerance for potable water at 0.1 ppm is a part of this request.

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:

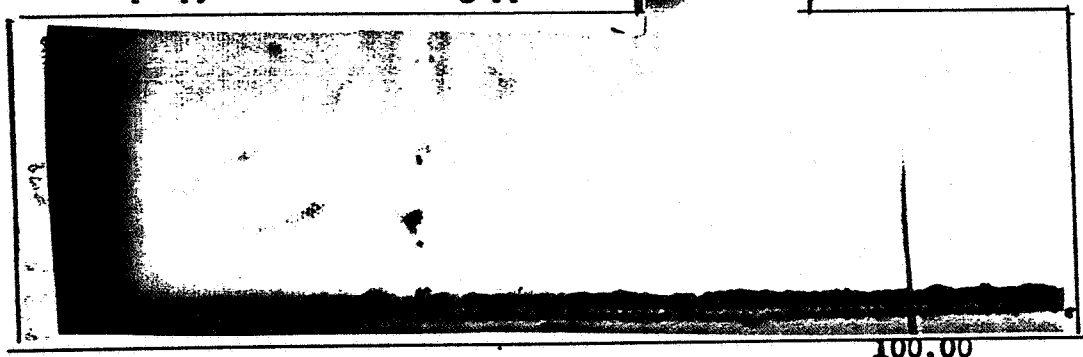
Formulation (Confidential)

Roundup

IngredientPercent Weight

Isopropylamine salt of glyphosate

41.00



100.00

INERT INGREDIENT INFORMATION DELETED

Inerts cleared under 180.1001 (c) & (d).

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)
- °Teratology (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 examined. As reported the study shows no oncogenic potential.
- ° Neurotoxicity (hen): negative at 7.5 gm/kg (cumulative for 3 days) (valid)
- ° Dominant Lethal (mice): negative at 10 mg/kg. (highest dose), supplement study, no records of positive controls.
- ° Host-Mediated Assay: negative (valid)
- ° Ames Test: negative (supplemental study), no raw data available
- ° Rec-Assay: negative (supplemental study), no raw data available

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

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.

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

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

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

- 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 10.93%. The current action utilizes the ADI to 19.01%. Therefore the current action utilizes 8.08% of the ADI. (Computer printout attached)
- 6) No regulatory actions are pending against the pesticide and no RPAR criteria have been exceeded.

Conclusions & Recommendations

The requested tolerances 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 re production study show that glyphosate has low potential for showing any teratology effects. The oncogenic potential of glyphosate is not fully elucidated. The lifetime mouse and rat 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.

W. H. Foster

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)	0.000	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

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

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)	0.200	1.42	0.00426
Olives(104)	0.100	0.06	0.00009
Stone Fruits(151)	0.200	1.25	0.00374

MPI	THRC	% ADI
3.0000 mg/day/60kg	0.3279 mg/day/1.5kg	10.93

Current Action 9F2163, 9H5204

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
Potable water(198)	0.100	133.33	0.20000

MPI

TMRC

ADI

3.0000 mg/day/60kg

0.5704 mg/day/1.5kg

19.01
