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

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MAY 23 1980

MEMORANDUM

SUBJECT: EPA Reg.#524-308 (Roundup); Glyphosate; PP#0F2329; petition proposing a tolerance for the combined residues of glyphosate N-(phosphonomethyl)glycine and its metabolite, aminomethylphosphonic acid in or on peanuts at 0.1 ppm, peanut forage/hay at 0.3 ppm, and peanut shells at 0.4 ppm. CASWELL#661A

WDB 4/11/80

FROM : William Dykstra
Toxicology Branch, HED (TS-769)

TO : Robert Taylor
Product Manager#25
Registration Division (TS-767)

& Residue Chemistry Branch
(TS-769)

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

Recommendations:

1) The requested tolerances can be toxicologically supported.

2) The recommendations of the "free-standing" summary are contained herein.

Section F - Proposed Tolerances

This petition requests that a tolerance for the combined residues of glyphosate N-(phosphonomethyl)glycine and its metabolite, aminomethylphosphonic acid, be established for peanuts as follows:

Commodity	Proposed Tolerance
Peanut	0.1 ppm
Forage/Hay	0.3 ppm
Shells	0.4 ppm

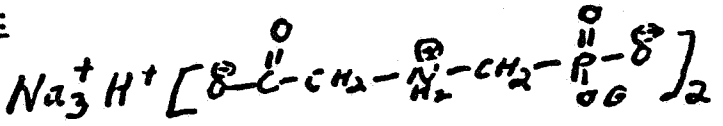
A. Substance Identification

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

2. Synonyms: Glyphosate, Roundup

3. Purity of Technical Material: 95-98%

4. Structure:



Formulation: EPA Reg.#524-308 (Confidential)

Ingredient	Percent Weight
Isopropylamine salt of glyphosate	41.00
[redacted]	
	100.00

INERT INGREDIENT INFORMATION DELETED

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 LD_{50} 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 a 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), supplemental study, no records of positive control.
- Host-Mediated Assay: negative (valid)
- Ames Assay: negative (supplemental study) no raw data available
- Rec-Assay: negative (supplemental study) no raw data available.

2) Memo of 9/22/79 from Merry Lou Alexander to Product Manager#25. Glyphosate was not mutagenic in the following test systems.

   (a) Rec-Assay in two strains of B. subtilis up to 2000 ug test material/disk.

   (b) Reverse mutation in five histidine - requiring strains of S. typhimurium and one tryptophan - requiring of E. coli, with or without metabolic activation.

   (c) Ames test in four strains of Salmonella, with or without metabolic activation.

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

4) 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

5) Tolerances have been established under 40 CFR 180.364.

6) The published tolerances utilize 6.93% of the ADI. Ubpublished, TOX approved tolerances utilize the ADI to 19.01%. The current action utilizes 0.02% of the ADI. All tolerances on glyphosate utilize 19.03% of the ADI (computer printout attached).

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

Conclusions and 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 reproduction study show that glyphosate has low potential for showing any teratogenic effects.

The oncogenic potential of glyphosate is not fully elucidated. The life-time mouse and rat studies, however, provide assurance that glyphosate has a relatively low oncogenic potential.

A further assurance of low risk with glyphosate is found in the fact that on a theoretical basis the exposure via the diet is about one-fifth of the ADI at present.

TOX/HED:th:CFRICK:4-10-80 C. Frick 4/11/80