

US EPA ARCHIVE DOCUMENT



Glyphosate / Tox

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

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releasable

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

FEB 3 1981

SUBJECT: EPA Reg.#524-308; Roundup (Glyphosate); PP#OF2422
Glyphosate in or on forage grasses and forage legumes.
CASWELL#661A; Accession#099625

FROM: William Dykstra, Toxicologist
Toxicology Branch, HED (TS-769) WMD JDC 1/16/81

TO: Robert Taylor (25)
Registration Division (TS-767)
and
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

Recommendations:

- 1) The requested tolerances can be toxicologically supported.
- 2) The following studies are currently lacking and are required to be submitted:
 - a) oncogenicity - 2 species

Section F

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

<u>Commodity</u>	<u>Proposed Tolerance</u>
Forage legumes	0.4 ppm
Forage grasses	0.2 ppm

A. Formulation to be used is Roundup (EPA Reg.#524-308). Inerts are 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 mg/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) (repeated 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 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) Memo of 1/16/81 from William Dykstra to R. Taylor.

(a) Rat Teratology: Severe maternal toxicity at 3500 mg/kg/day.
Negative at 3500 mg/kg/day; Fetotoxic NOEL =
1000 mg/kg/day

(b) Rabbit Teratology: Negative at 350 mg/kg/day; Fetotoxic NOEL =
175 mg/kg/day.

(c) Mouse Dominant Lethal Assay: Negative at 2000 mg/kg.

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

5) 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.

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

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

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

6) Tolerances have been established under 40 CFR 180.364.

7) The published tolerances utilize 6.93% of the ADI. Unpublished, TOX approved tolerances utilize the ADI to 19.03%. The current action does not utilize any of the ADI.

8) 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.

The following studies are currently lacking and are required to be submitted:

a) oncogenicity - 2 species

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.

TS-769:TOX/HED:th:LCHITLIK:1-16-81

File last updated 4/8/80

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
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

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

CROP	Tolerance	Food Factor	mg/day/1.5kg
Sugar, cane&beet(154)	1.000	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

Current Action PP9F2163, 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
Potable Water(198)	0.100	133.33	0.20000
Peanuts(115)	0.100	0.36	0.00054

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MPI

TMRC

% ADI

3.0000 mg/day/g

0.5709 mg/day/1.5kg

19.03

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