

US EPA ARCHIVE DOCUMENT



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

✓ OK

4/2/81

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Glyphosate; PP#1E2490; Glyphosate in/on Mangoes
CASWELL#661A Accession#099956

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

TO: Clint Fletcher (43)
Registration Division (TS-767)
and
Residue Chemistry Branch
Hazard Evaluation Division (TS-769) WJB

Recommendations:

- 1) The requested tolerance can be toxicologically supported.
- 2) The following studies are currently lacking and are required to be submitted within a reasonable period of time:
 - a) oncogenicity - 2 species
- A. Formulation to be used is Roundup (EPA Reg.#524-308). Inerts are cleared under 180.1001.
- B. Section F: Proposed tolerance for the pesticide chemical Glyphosate in or on Mangoes.

The petitioner, IR-4 National Director, Dr. R.H. Kupelian, on behalf of the IR-4 Technical Committee and the Agricultural Experiment Stations of Florida and Puerto Rico requests the establishment of a tolerance for combined residues of Glyphosate and its metabolite aminomethylphosphonic acid resulting from herbicide application of the isopropylamine salt of Glyphosate in or on the raw agricultural commodity mangoes at 0.2 ppm.

Review:

1) Memo of 8/22/78 from R. Engler to R. Taylor. Toxicology Branch has reviewed the validated studies in support of Glyphosate.

a) 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 (higher 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 (supplemental study) no raw data available.
- °Rec-Assay: Negative (supplemental study) no raw data available.

2) Memo of 9/22/79 from M.L. 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 strain 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 W. 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: 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) No regulatory action are pending against the pesticide.
- 8) The published tolerance utilize 7.21% of the ADI. Unpublished, Tox approved tolerances utilize the ADI to 19.73%.

The current action does not utilize any of the ADI. All tolerances on Glyphosate utilize 19.73% of the ADI. (computer printout attached).

Conclusions and Recommendations:

The requested tolerance can be toxicologically supported.

The oncogenic potential of Glyphosate is not fully elucidated. The chronic rat and mouse feeding 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:th:TOX/HED:WDykstra:4-2-81:#4

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PP 100.364 Glyphosate Roundup -/2/81

File last updated 4/2/81

ACCEPTABLE DAILY INTAKE

ADI, 18yr (60kg)	100	1	100
mg/kg/day	100	mg/kg/day	mg/day (60kg)
3.000	100.00	0.050	3.0000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Cottonseed (41)	6.000	0.15	0.01350
Grain Crops (64)	0.100	13.79	0.02069
Avocados (6)	0.200	0.03	0.00009
Citrus Fruits (33)	0.200	3.61	0.01144
Coffee (36)	1.000	0.75	0.01119
Grapes, inc raisins (66)	0.100	0.49	0.00074
Leafy Vegetables (80)	0.200	2.76	0.00628
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
Seeds/Fod 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
Asparagus (5)	0.200	0.14	0.00043
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

HPI 3.0000 mg/day (60kg) TMRC 0.2163 mg/day (1.5kg) ADI 7.21

Unpublished, Tox Approved PP#8E2122,9H5196,9F2163,9H5204,0F2329,0E2421,1E2443,1L2444
IF2455

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Sugar, cane/beet (154)	1.900	3.64	0.10369
Molasses (96)	18.000	0.03	0.00628
Cucurbits (49)	0.100	2.84	0.00426
Fruiting vegetables (80)	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	1.6	0.03250
Potato water (198)	0.100	133.33	0.20000
Peanuts (115)	0.100	0.30	0.00054
Cranberries (44)	0.200	0.03	0.00009
Guava (154)	0.200	0.03	0.00009
Papayas (109)	0.200	0.03	0.00009
Cottonseed (41)	9.000	0.15	0.02025

HPI 3.0000 mg/day (60kg) TMRC 0.5919 mg/day (1.5kg) ADI 19.73

Current Action PF#1E2490

CROP	tolerance	Food Factor	µg/day (1.5kg)
Diangoes (do)	0.200	0.3	0.00009

MI	THRC	AL1
3.0000 mg/day (60kg)	0.5920 mg/day (1.5kg)	19.73
