

RELEASABLE



GLYPHOSATE / Tox
 UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
 WASHINGTON, D.C. 20460

MEMORANDUM:

7/2/86

SUBJECT: EPA Reg. No. 524-308; Roundup; PP# 6F3408;
 Glyphosate in/on Sunflowers at 0.10 ppm;

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES"Free Standing" Summary

Caswell No. 661A
 Project No. 1882/1883
 Record No. 172912/174111
 Assessment No. 262632

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

THRU: Edwin Budd, Section Head
 Review Section II
 Toxicology Branch
 Hazard Evaluation Division (TS-769)

FROM: William Dykstra
 Toxicology Branch
 Hazard Evaluation Division (TS-769)

William Dykstra 7/2/86

1. The data available in considering the tolerance include:

- o Rat oral LD₅₀ : 4320 mg/kg (M+F)
- o Rabbit teratology : Negative: 350 mg/kg (HDT)
- o Rat teratology : Negative: 3500 mg/kg (HDT)
- o 3-generation rat reproduction : NOEL = 10 mg/kg/day
- o 26-month rat feeding study : Oncogenic potential: negative
NOEL = 31 mg/kg/day (HDT)
- o 2-year oncogenic mouse feeding study: Oncogenic potential: indeterminate
at 30,000 ppm (HDT)
- o Multi-test mutagenic studies : Negative
- o One-year dog study : Tentative NOEL = 20 mg/kg/day

2. No data are currently lacking. However, based on the SAP review of the oncogenic potential of glyphosate, it was concluded that "there be a data call-in for further studies in rats and/or mice to clarify unresolved questions." A repeat

of the chronic/oncogenic rat feeding study at dosages corresponding to the maximum tolerated dose and a repeat of the mouse oncogenicity study will be required to further address the MTD questions relating to the oncogenicity of glyphosate.

3. The registrant will be informed of these repeat studies.

4. Tolerances have been established for the combined residues of glyphosate and its metabolite aminomethyl phosphonic acid in several raw agricultural commodities (40 CFR 180.364).

5. Published tolerances utilize 24.19% of the ADI. Unpublished, Tox. approved tolerances utilize the ADI to 25.52%. The current action utilized 0.0007% of the ADI and contributes 0.000045 mg/day to the TMRC. All tolerances utilize 25.52% of the ADI.

6. The ADI is based on the NOEL of 10 mg/kg/day in the 3-generation rat reproduction study. A 100 fold safety factor was utilized in calculating the ADI.

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

$$ADI = 10 \text{ mg/kg/day} \times \frac{1}{100}$$

$$ADI = 0.10 \text{ mg/kg/day}$$

The MPI is 6.0 mg/day for a 60 kg person.

7. There are no pending regulatory actions against registration of the pesticide.

8. The Agency recently requested the SAP to consider the potential oncogenicity of glyphosate. In their 2/24/86 report, the SAP concluded that "glyphosate be categorized as Group D (not classified) and that there be a data call-in for further studies in rats and/or mice to clarify unresolved questions."

- 3 -

If the Agency concurs with the SAP position, glyphosate may not be considered oncogenic in male mice. If this is the case, the Delaney clause may not apply to 409 tolerances for glyphosate.

Depending of the Agency's position relative to the SAP conclusions, the requested tolerances may or may not be toxicologically supported.