



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

MEMORANDUM:

6/24/86

SUBJECT: Roundup; EPA Reg. No. 524-308; PP#3F2809/5H5450;
glyphosate in/on wheat; "Free Standing" Summary
Caswell No. 661A
Project No. 1273/1274/1275
Record No. 165735/165738/165731

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

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

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

Budd
6/22/86

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

William Dykstra 6/19/86
file for URB 6/24/86

1. The data available in considering the tolerances 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 23.73% of the ADI.

The current action utilizes 0.52% 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."

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.

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