



Glyphosate / Tox

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

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Caswell file
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MEMORANDUM

SUBJECT: Glyphosate; EPA Reg. #: 524-308;
Revised Section F; PP# 3F2809, 5H5450;
Glyphosate in/on Wheat
Caswell #: 661A
Accession #: 073100

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

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

and
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

THRU: *[Signature]* 3/18/85
Robert P. Zendzian, Ph.D.
Acting Head, Review Section IV
Toxicology Branch
Hazard Evaluation Division (TS-769)

FROM: William Dykstra, Ph.D. *William Dykstra*
Toxicology Branch
Hazard Evaluation Division (TS-769) 3/12/85
[Signature] 3/19/85

Action Requested:

Evaluate petition request for the use of glyphosate in/on wheat.

Recommendations:

1. Glyphosate is oncogenic to male mice. Renal tubule adenomas which are both dose-related and compound-related have been identified. A consensus review of this study is attached.

In light of these findings, 409 (H, food additive) tolerances can not be toxicologically supported due to the Delaney rule.

Background:

- o Teratology - rat - negative at 3500 mg/kg/day;
fetotoxic NOEL was 1000 mg/kg/day;
- o Teratology - rabbit - negative at 350 mg/kg/day;
fetotoxic NOEL was 175 mg/kg/day;
- o Mutagenicity - negative in the following studies:

- a. Rec-assay in two strains of B. subtilis up to 2000 ug/test.
- b. Reverse Mutation in 5 histidine - requiring strains of S. typhimurium and 1 tryptophan- requiring strain E. coli, with and without metabolic activation .
- c. Ames test in four strains of Salmonella, with and without metabolic activation.
- d. Dominant lethal study in the mouse at 2000 mg/kg.
- o Three-generation reproduction - rat - NOEL of 10 mg/kg/day based on pathological findings of renal focal tubular dilation in high dose male F_{3b} weanlings.
- o Chronic/oncogenic - rat - NOEL was 31 mg/kg/day; oncogenic potential was negative.

Review:

1. Proposed tolerances

Tolerances are established for combined residues of glyphosate and its metabolite aminomethylphosphonic acid on grain crops which includes wheat.

40 CFR 180.364

Grain Crops.0.1(N)
Forage grasses0.2

When used as directed on the requested wiper applicator label, the wheat tolerances will need to be the following:

Wheat grain 0.25 ppm
Wheat straw 0.35 ppm

21 CFR 561.253

When used as directed on the requested wiper applicator label, a food additive tolerance will be needed for:

Wheat bran. 0.4 ppm
Wheat shorts. 0.4 ppm

- 2. No new toxicity data were submitted.
- 3. The formulation to be used is Roundup (EPA Reg. No. 524-308-AA; Inerts are cleared under Section 180.1001).