



*Glyphosate / Tox*

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

MEMORANDUM

MAR 3 1983

RELEASABLE

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

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

THRU: Orville E. Paynter, Ph.D.  
Chief, Toxicology Branch  
Hazard Evaluation Division (TS-769) *wsb*

SUBJECT: Glyphosate (Roundup®) on Wheat; PP#3F2809; Reg.#524-308  
CASWELL#661A

Recommendations:

a) ~~Consideration~~ of this action (0.2 ppm on wheat) should be delayed pending reevaluation of thyroid slides from the 2-year rat study and possibly also delayed pending evaluation of an oncogenic study in a second species. If the tentative conclusion that no oncogenic effect was demonstrated (memo dated 2-10-83 from Dykstra to Taylor) is supportable after rereading the rat slides, this action may be toxicologically supported.

b) Chronic (and subchronic) oral toxicity data in a non-rodent species and an oncogenic study in a second species are data gaps.

Review:

1. Action Requested:

This petition requests the establishment of a tolerance in/on wheat of the herbicide glyphosate (N-phosphonomethyl glycine) and its metabolite, aminomethylphosphonic acid, at 0.2 ppm.

This represents an increase of 0.1 ppm in/on wheat, since 0.1 ppm on grain crops, including wheat, has already been established.

2. The formulation to be used will be Roundup® (MON-2139). Inerts are cleared under 180.1001.

3. Toxicological Studies:

No new data were submitted. Studies supporting this action are listed in a memo on Glyphosate (dated 9-3-82 from Teeters to Taylor); since then the two IBT subchronic oral toxicity studies (#B-1020, rat and #B-1021, dog) and the rat reproduction study (IBT#B-566) mentioned in the referenced memo have been evaluated and declared invalid.

Recently (memo dated 2-10-83 from Dykstra to Taylor) a question has arisen concerning the significance of the incidence of C-cell carcinomas of the thyroid in female rats in the lifetime feeding study in this species with Glyphosate, and the thyroid slides will be reevaluated; the tentative conclusion reached is that Glyphosate was not oncogenic in that study.

Current data gaps include chronic (and subchronic) toxicity in a non-rodent species and an oncogenic study in a second species.

4. Many tolerances have been established under 40 CFR 180.364; the one for grain crops, including wheat, is 0.1 ppm.

5. Evaluation of the ADI:

Based on a NOEL of 10 mg/kg/day in the reproduction study (Bio/dynamic, 9-18-81) and using a safety factor of 100, the ADI is 0.1 mg/kg/day ( $10 \text{ mg/kg/day} \times \frac{1}{100} = 0.1 \text{ mg/kg/day}$ ). The MPI for a 60 kg person is 6 mg/day.

6. The published tolerances utilize 5.90% of the ADI. Total published and unpublished, but Tox. approved, tolerances utilize 23.73% of the ADI. All tolerances, including the one in this action (contribution of 0.01554 mg/day to the TMRC) utilize 23.99% of the ADI and the TMRC is 1.4393 mg/day, based on a 1.5 kg diet. This action increases the TMRC by 1.09%.

7. No regulatory actions are pending against the pesticide and no RPAR criteria have been exceeded.

8. Other relevant considerations:

Concentrations of 0.2-0.4 ppm of N-nitroso-glyphosate (NNG) are present in the formulated product (memo of 12-2-77 from RCB, PP#7F1971/FAP 7H5168) and there are three IBT studies with NNG which are yet to be evaluated (2-year orals in rat and dog and a rat reproduction). No detectable residues of NNG were found in soybean grain, forage and hay or in cottonseed using an analytical method sensitive to 0.02 ppm. Similar results would be expected with this use on wheat, particularly since the herbicide is not to be applied directly to the wheat plant (personal conversation with R. Loranger, RCB). No problem of serious toxicological concern is anticipated.

9. Conclusion:

a) Consideration of this action (0.2 ppm on wheat) should be delayed pending reevaluation of thyroid slides from the 2-year rat study and possibly also delayed pending evaluation of an oncogenic study in a second species. If the tentative conclusion that no oncogenic effect was demonstrated (memo dated 2-10-83 from Dykstra to Taylor) is supportable after rereading the rat slides, this action may be toxicologically supported.

b) Chronic (and subchronic) oral toxicity in a non-rodent species and an oncogenic study in a second species are data gaps.

*Winnie Teeters* *LOC 2/25/83*  
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File last updated 2/18/83

## ACCEPTABLE DAILY INTAKE DATA

NOEL change recorded per

| RAT, Older | NOEL   | S.F. | ADI       | MPI           |
|------------|--------|------|-----------|---------------|
| mg/kg      | ppm    |      | mg/kg/day | mg/day (60kg) |
| 10.000     | 200.00 | 100  | 0.1000    | 6.0000        |

## 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        |
| Grapes, inc raisins ( 66) | 0.100     | 0.49        | 0.00074        |
| Leafy Vegetables ( 80)    | 0.200     | 2.76        | 0.00828        |
| 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        |
| Palm Oil (202)            | 0.100     | 0.03        | 0.00005        |
| Pistachio nuts (210)      | 0.200     | 0.03        | 0.00009        |
| 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        |
| Sugar, cane & beet (154)  | 2.000     | 3.64        | 0.10915        |
| Molasses ( 96)            | 20.000    | 0.03        | 0.00920        |
| Cranberries ( 44)         | 0.200     | 0.03        | 0.00009        |
| Cottonseed (oil) ( 41)    | 15.000    | 0.15        | 0.03375        |
| Kidney (203)              | 0.500     | 0.03        | 0.00023        |
| Liver (211)               | 0.500     | 0.03        | 0.00023        |
| Peanuts (115)             | 0.100     | 0.36        | 0.00054        |
| Guava (184)               | 0.200     | 0.03        | 0.00009        |
| Papayas (109)             | 0.200     | 0.03        | 0.00009        |
| Mangoes ( 88)             | 0.200     | 0.03        | 0.00009        |
| Soybeans (oil) (148)      | 6.000     | 0.92        | 0.08263        |
| Pineapple (123)           | 0.100     | 0.30        | 0.00044        |
| Fish, shellfish ( 59)     | 0.250     | 1.08        | 0.00406        |

| MPI                  | TMRC                  | % ADI |
|----------------------|-----------------------|-------|
| 6.0000 mg/day (60kg) | 0.3543 mg/day (1.5kg) | 5.90  |

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Unpublished, Tox Approved 9F2163, 2329, 2680, 1E2444, 9H5204, 2G2686, 1H5310

| 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        |
| Potable Water (198)        | 0.500     | 133.33      | 1.00000        |
| Soybeans (oil) (148)       | 4.000     | 0.92        | 0.05509        |
| Tea (162)                  | 4.000     | 0.07        | 0.00429        |
| Coconut ( 35)              | 0.100     | 0.03        | 0.00005        |

| MPI                  | TMRC                  | % ADI |
|----------------------|-----------------------|-------|
| 6.0000 mg/day (60kg) | 1.4238 mg/day (1.5kg) | 23.73 |

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Current Action 3F2809

| CROP        | Tolerance | Food Factor | mg/day (1.5kg) |
|-------------|-----------|-------------|----------------|
| Wheat (170) | 0.100     | 10.36       | 0.01554        |

| MPI                  | TMRC                  | % ADI |
|----------------------|-----------------------|-------|
| 6.0000 mg/day (60kg) | 1.4393 mg/day (1.5kg) | 23.99 |

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