5395
(13)

Glyphosate / Tox

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

RELEASABLE

MEMORANDUM MAR 3 1983

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 mg/kg/day x $\frac{1}{100}$ = 0.1 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 2/25/83

Winnie Teeters, Ph.D.
Toxicology Branch
Hazard Evaluation Division (TS-769)

TS-769:th:TOX/HED:WTeeters:2-24-83:card 1

CFR 180.36 Glyphosate Roundup 2/18/83

File last updated 2/18/83

NOEL change recorded per

ACCEPTABLE DAILY INTAKE DATA

RAT,Older NOEL mg/kg	ppm	S.F.	ADI mg/kg/day	MPI 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(164)	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

****

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

****

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

****