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DATE: May 14, 1974

- Mr. Lee TerBush, Acting Chief
Coordination Branch
Registration Division (HM-567)

Registration No.: 524-EXP-X

Product Name: Roundup

Action Requested: Experimental Permit

Registrant: Monsanto Company

Related Petitions: 4G1444

Formulation:

Active Ingredient:

41.0% N-phosphonomethyl glycine, isopropylamine salt

Inert Ingredients:

[Redacted area]

- * Cleared under CFR 40 Sec. 180.1001(c)
** Cleared under CFR 40 Sec. 180.1019
*** Not cleared under CFR 40 Sec. 180.1001

Use: Herbicide for non-selective weed
control in corn, cotton, soybeans
and wheat cropping systems

Application Rate: one to five quarts per acre

Application Frequency: two to three times per year

Application Method: spray

Limitation: ten quarts per acre per crop

Summary Toxicological Evaluation

Acute Studies:

<u>Species</u>	<u>Route</u>	<u>Formulation</u>	<u>LD₅₀ or dose</u> <u>mg/kg</u>	<u>Observations</u>
Rat (M&F)	Oral	Technical	4320 (3930-4750)	Lethargy, diarrhea, weakness, collapse. Hemorrhagic lungs and liver. GI inflammation.
Rabbit (M&F)	Oral	Technical	3899 (2836-5092)	Hypoactivity in 1 hr to 10 days. Death in 3-11 days.
Rat (M&F)	Oral	30% 41%	4900 (4440-5400)	Same as for technical
Rat (M&F)	Oral	41%	4040 (3660-4460)	Same as for technical
Rabbit (M&F)	Dermal	Technical	>7940	No signs of systemic toxicity
Rabbit (M&F)	Dermal	30% 41%	>7940	Hypoactivity
Rat (M&F)	Inhalation (4 hrs)	41%	>12.2 mg/l	No signs of systemic toxicity
Rabbit (M&F)	Skin irritation (24-hr exposure)	Technical	0.5 gm	No-irritating score 0/8
Rabbit (M&F)	Skin irritation (24-hr exposure)	30% 41%	0.5 ml	Mild irritant, score 2.3/8
Rabbit	Eye irritation (24-hr exposure)	Technical	100 mg	Slight irritation max. score 12.6/110 in 1 hr.
Rabbit	Eye irritation (24-hr exposure)	30% 41%	0.1 ml	Severe irritant, max. score 64.3/110 in 7 days. Corneal opacity and ulceration.

(Table continued)

Summary Toxicological Evaluation (continued)Acute Studies (continued):

<u>Species</u>	<u>Route</u>	<u>Formulation</u>	<u>LD₅₀ or dose mg/kg</u>	<u>Observations</u>
Rabbit	Eye irritation (15 min. exposure)	30% 41%	0.1 ml	Mild irritation, max. score 16/110 in 1 hr. Normal in 7 days.
	(30 min. exposure)	30% 41%	0.1 ml	Mild irritation, max. score 15.3/110 in 1 hr. Normal in 7 days.
	(15 min. exposure)	5%	0.1 ml	Slight irritation, max. score 12/110 in 1 hr. Normal in 7 days.
	(30 min. exposure)	5%	0.1 ml	Slight irritation, max. score 12.6/110 in 1 hr. Normal in 7 days.
	(24 hr. exposure)	5%		Slight irritation, max. score 11.3/110 in 1 hr. Normal in 7 days.
*Rat (M&F)	Oral		8300 (7300- 9460)	Same as for technical
*Rabbit (M&F)	Skin irritation	Moistened with water	0.5 gm	Score 0.0
*Rabbit (M&F)	Eye irritation		100 mg	Slight irritant max. score 10/110 in 1 hr.

Subacute Studies:

21-Day Rabbit Dermal (~~30%~~^{41%} formulation of Roundup): NEL <37.9 mg/kg

The use concentration produced red well-defined erythema, moderate edema, superficial escharosis and pustules. Hemorrhaging was reported.

21-Day Rabbit Dermal (~~30%~~^{41%} formulation of Roundup): NEL <75.8 mg/kg

Moderate to marked dermal irritation and slight to moderate deleterious effects on testes were evident.

* Acute Studies on Major Metabolite - aminomethylphosphonic acid

Human Patch Test (1:45 dilution): Non-irritating

90-Day Dog Feeding (Tech): NEL >2000 ppm

90-Day Rat Feeding (Tech): NEL >2000 ppm

Mice Mutagenic (Tech): Not mutagenic

Rabbit Teratogenic (Tech): Not teratogenic

Mice Carcinogenic (Tech): Not carcinogenic

3-Generation Rat Reproduction: NEL >300 ppm

Rabbit Metabolism: 25 to 52% of material is excreted in 24 hours;
90% in 5 days with 80% in feces and 10% in the
urine. Only the glycine moiety appears as
tissue residue.

Rat Metabolism: 82 to 98% of material is excreted in 48 hrs; 99% in
120 hrs. Tissue retention after 120 hrs is approximately
1% glycine labeled materials in the muscle and methylene
labeled material in the gut. The parent compound remained
unchanged and is excreted in urine and feces.

Aminomethyl phosphonic acid and methylaminomethyl phos-
phonic acid were reported to be impurities and not
metabolites.

Conclusion

We cannot recommend further action on the registration of this product
until the following items are finalized:

- 1) Clear [redacted] as an inert
- 2) Clear [redacted] an inert
- 3) Change the signal word "Warning" to read "Danger" (due to
eye damage)

INERT INGREDIENT
INFORMATION DELETED

- 4) Change the statement "Avoid contact with eyes, skin or clothing" to read "Do not get in eyes, on skin or on clothing."

Robert D. Coberly

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cc:
Div. File
Br. File

RDCoberly/ccw
5/14/74