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ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Date: May 24, 1973

003853

Reply to Attn of:

Subject:

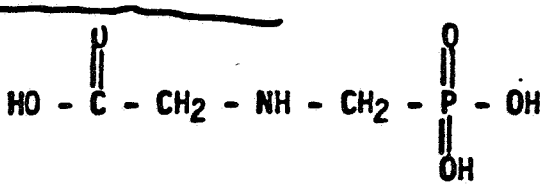
To: Mr. Lee E. TerBush, Acting Chief
Coordination Branch
Registration Division

Registration No.	:	524-GNI
Product Name	:	Roundup
Registrant	:	Monsanto Company
Use	:	A postemergence herbicide for control of annals, perennial grasses and broadleafed weeds.
Application Area	:	Railroad, pipeline, highway rights-of-way, petroleum tank farms, pumping installations, roadsides, storage areas, lumber yards, fencerows, industrial plant sites, parking areas, airports, around building foundations, sidewalks, fences, shelterbelts, driveways, around swimming pools, tennis courts, spot treatment in lawns.
Application Rate	:	0.5 to 4 quarts per acre- one or two applications as needed.
Application Method	:	Spray

PHYSICAL AND CHEMICAL DATA

Name: N-phosphonomethyl glycine

Structure:



Impurities: Sulfuric acid and phosphoric acid are the major impurities in the technical product.

Solubility: Soluble in water (1% at 25°C). Insoluble in ethanol, acetone, and benzene.

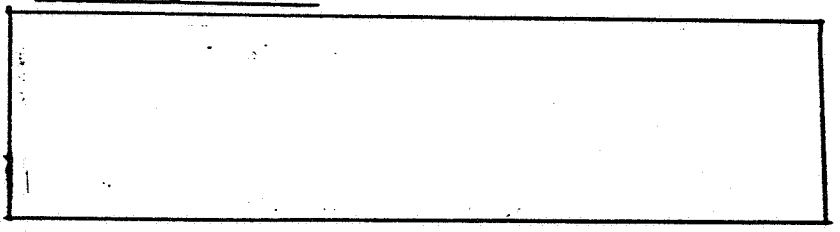
Form: Crystalline solid (Tech)

Formulation: Roundup

41.0% Glyphosate (N-phosphonomethyl glycine), isopropylamine salt.

Inert Ingredients

INERT INGREDIENT INFORMATION DELETED



ACUTE TOXICITY

Rat Oral LD_{50} - Younger Lab - September 18, 1970

The test material, identified as CP-67573-3, was administered as a 25% aqueous solution-suspension.

Results

LD_{50} = 4320 mg/kg

Rabbit Dermal MLD - Younger Lab - September 18, 1970

The test material, identified as CP67573-3, was applied as a 50% aqueous suspension to intact test sites only. Only one male and one female were used in the entire study.

Results

MLD = greater than 7940 mg/kg in females and greater than 5010 mg/kg in males.

Rabbit Dermal Irritation - Younger Lab - 9/18/70

The test material, identified as CP-67573-3, was applied as a moistened powder to intact test sites only. Three rabbits of each sex were used. Exposure time was 24 hours.

Results

No irritation was observed.

Rabbit Eye Irritation - Younger Lab - 9/18/70

The test material, identified as CP-67573-3, was applied undiluted to the conjunctival sac of three rabbits. The eyes were washed at 24 hours post treatment.

Results

No irritation was observed.

Rabbit Oral LD_{50} - Industrial Bio-Test Lab - 12/6/72

The test material identified as CP-67573, was administered as a 35% (w/v) suspension in methylcellulose. Two rabbits of each sex were used per dosage level.

Results

LD_{50} = 3,800 mg/kg

Rat Oral LD_{50} (3 lbs/gal. formulation) - Younger Lab - 10/7/71

The test material, identified as CP-70139, formulation 3 lbs/gal. was administered undiluted. Five rats (mixed sex) were used per level in a range of from 3160 to 6310 mg/kg.

Results

LD_{50} = 4900 mg/kg. Lung hyperemia, liver discoloration and acute gastrointestinal inflammation were noted.

Rabbit Dermal MLD (3 lbs/gal. formulation) - Younger Lab - 10/7/71

The test material, identified as CP-70139, was applied undiluted to intact test sites only. Length of exposure was 24 hrs.

Results

MLD greater than 7940 mg/kg.

Rabbit Dermal Irritation (3 lbs/gal. formulation) - Younger Lab -10/7/71

The test material, identified as CP-70139, was applied undiluted to intact test sites. Length of exposure was 24 hours.

Results

The average maximum score was 2.3 out of a possible 8 at 24 hrs. No irritation was noted at 120 hours. These results indicate the chemical is as a mild irritant.

Rabbit Eye Irritation (3 lbs/gal. formulation) - Younger Lab-10/7/71

The test material, identified as CP-70139, was applied undiluted to the eye. The eyes were washed after 24 hours.

Results

The average maximum score was 64.3 of a possible 110 at seven days. Slight corneal ulceration was noted at 10 days. The data show the formulation to be a severe eye irritant. Category I label precautionary are required.

Rabbit Eye Irritation (3 lbs/gal. formulation) - Younger Lab-10/27/71

PART I

The test material, identified as CP-70139 formulation, was applied undiluted. Eyes were washed 15 or 30 minutes post treatment.

PART II

The test material was applied as a 5.0% aqueous solution. Eyes were washed 15 minutes, 30 minutes or 24 hours.

Results

a) The 15 minute exposure to the undiluted material produced an average maximum score of 16 out of a possible 110. This score indicates a mild eye irritant.

b) The 30 minute exposure to the undiluted material produced an average maximum score of 15.3 out of a possible 110. This score indicates a mild eye irritant.

c) The 15 minute exposure to the 5.0% aqueous solution produced an average maximum score of 12.0 out of a possible 110. This score indicates a slight eye irritant.

d) The 30 minute exposure to the 5.0% aqueous solution produced an average maximum score of 12.6 out of a possible 110. This score indicates a slight eye irritant.

e) The 24 hour exposure to the 5.0% aqueous solution produced an average maximum score of 11.3 out of a possible 110. This score indicates a slight eye irritant.

Rat Oral LD_{50} - Younger Lab - 10/2/72

The test material, identified as MON-2139, was tested undiluted. Five rats (both sexes) were used per level.

Results

LD_{50} = 4040 mg/kg

Rat Inhalation LC_{50} - Industrial Bio-Test Lab - 11/7/72

The test material was identified as MON-2139. Five rats of each sex were exposed to a nominal chamber air concentrate of 12.2 mg/L for four hours.

Results

LC_{50} is greater than 12.2 mg/L. No mortality occurred.

SUBACUTE TOXICITY

Mice Mutagenic - Industrial Bio-Test - 1/24/72

The material tested was identified as CP-67573 and was administered as a 0.1% solution in corn oil.

Twelve male mice from the Charles River strain received a single IP injection of the test material at the level of 5.0 or 10 mg/kg. Ethyl methanesulfonate served as a positive control.

Each of the treated males was mated to three virgin females immediately after dose administration. The females were replaced by another three virgin females after each seven days for a total of six weeks.

The males were sacrificed following the sixth week of mating. The females were sacrificed approximately one week after the mating period.

Observations and tests for effects included implantation site count, resorption site count, and embryo count.

Deciduomata occurred at the sites of implanted blastocysts which failed to develop following implantation. Thus the mutagenicity of a chemical can be measured by the proportions of all implantations which are deciduomata.

Results

These data indicate the test material did not cause a dominant lethal response at 5 and 10 mg/kg.

Rabbit Teratogenic - Industrial Bio-Test Lab - 6/30/72

The test material was identified as CP-67573. Seventeen female New Zealand albino rabbits were used per level of 10 and 30 mg/kg. Thialidomide served as the positive control (37.5 mg/kg/day). All pregnant does were treated from Gestation Days 6 through 18 and sacrificed on Gestation Day 29. The young were removed by caesarian section.

Observations and tests for effects included body weight for the parents and viability, respiratory movements, body weight, paw movements, skeletal tissue examination and complete examination of major organs of all the young. The Hurley (Supplement to Teratology Workshop Manual, Berkeley, California, January 25-30, 1965, pages 121-122) method for skeletal tissue examination was employed.

Results

No external abnormalities were observed among the 10 mg/kg fetuses. One fetus of the 30 mg/kg level exhibited underdeveloped nares, parrot mouth, unicorn and no eyes. A second fetus showed an umbilical hernia which was considered unrelated to the administration of CP-67573.

The positive control group revealed thirty-four early resorption sites and six abnormal fetuses (6 bilateral talipomanus and 1 umbilical hernia).

These findings reveal that the chemical used in this study did not induce a teratogenic response.

90-Day Dog Feeding - Industrial Bio-Test Lab Inc. - 6/19/72

The test material, identified as CP-67573, was incorporated directly into the stock diet. Four dogs of each sex were used per level of 0, 200, 600, and 2000 ppm.

Observations and tests for effects included body weight, food consumption, clinical symptoms; at 0, 42, and 85 days the following determinations were conducted:

total leukocyte count	BUN
erythrocyte count	serum glucose
hemoglobin	serum alkaline phosphatase
hematocrit	SGOT
differential leukocyte count	SGPT
urine analyses	

Terminal data consisted of gross organ examination, organ weights of the liver, kidneys, heart, brain, spleen, gonads, adrenal, thyroid, and pituitary; histological examination of the following:

adrenal	gall bladder	muscle	small intestine
aorta	gonads	pancreas	spinal cord
bone marrow	heart	peripheral nerve	stomach
brain	kidneys	pituitary	thyroid
cecum	liver	prostate	trachea
colon	lungs	salivary gland	uterus
esophagus	lymph nodes	spleen	urinary bladder

Results

No significant abnormalities were observed at the levels tested. No effect level is 2000 ppm.

90-Day Rat Feeding - Industrial Bio-Test Lab Inc. - 6/26/72

The test material, identified as CP-67573, was mixed directly with the stock diet. Fifteen rats of each sex were used per level of 0, 200, 600, and 2000 ppm.

Observations and tests for effects included body weight, food consumption, mortality; at 0, 42, and 84 days the following determinations were conducted:

hematocrit	BUN
erythrocyte	SAP
hemoglobin	SGPT
total leukocyte count	glucose
differential leukocyte count	urine analysis

Terminal data consisted of organ weights of the liver, kidneys, spleen, gonads, heart and brain of each rat; the following tissues from ten rats of each sex from both the control and high level were microscopically examined:

esophagus	parathyroid	lung
stomach	spinal cord	lymph node
small intestine	uterus	skeletal muscle
urinary bladder	trachea	peripheral nerve
pituitary	cecum	bone
adrenal	colon	eye
testes	liver	optic nerve
seminal vesicle	salivary gland	brain
ovary	prostate	kidneys
bone marrow	heart	spleen
thyroid	aorta	pancreas

Results

Three deaths occurred during the study resulting from trama incurred during the collection of blood samples. No abnormalities were observed. The no-effect level for this study is 2000 ppm.

21-Day Rabbit Dermal (3 lbs/gal.) - Industrial Bio-Test Lab - 7/18/72

The test material studied was identified as MON-2139, 3 lbs/gal. EC, Lot XHC-33. Ten rabbits of each sex were used per level of 37.9 or 189.5 mg/kg. Half the test sites of each level were abraded. The test levels reflect the use concentration and 5 times the use concentration. Length of exposure was six hours per day per week. The concentrate of the test material was 1.64% and 8.20% v/v in water respectively for the dosage levels.

Observations and tests for effects included mortality, reactions, body weight, erythrocyte count, hemoglobin conc., hematocrit, BUN, serum alkaline phosphatase activity, SGPT, fasting blood glucose concentrate, urine analyses, weights of the brain, liver, kidneys, spleen, heart, gonads, adrenal, and thyroid; microscopic examination of the following tissues:

adrenal	liver	skeletal muscle
aorta	lungs	skin
brain	lymph nodes	small intestine
cecum	pancreas	spleen
colon	parathyroid	sternum
esophagus	pituitary	stomach
gall bladder	prostate	thyroid
gonads	peripheral nerve	trachea
heart	salivary gland	urinary bladder
kidney	seminal vesicle	uteri

Results

No mortality occurred at the 37.9 mg/kg level. Five deaths, 3 intact and 2 abraded test sites, occurred among the 189.5 mg/kg level rabbit between days 4-11. After the second and third week of treatment the test animals exhibited excitation and vocalization.

After four applications, the test material produced slight irritation at the 37.9 mg/kg level and moderate irritation at the 189.5 mg/kg level. By the 15th application, moderate to severe irritation was observed at the 37.9 mg/kg level and severe irritation at the 189.5 mg/kg level.

The low level test group revealed a reduced body weight gain; the high level animals lost body weight.

Statically significant increases in total leukocyte counts and in the percent of neutrophils and a decrease in percent of lymphocytes were noted. Gross changes at the test site included erythema, edema, superficial escharosis, pustules and hemorrhaging. Histopathologic exam revealed acanthosis, hyperkeratosis and dermatitis.

The no-effect level is less than 37.9 mg/kg. Category I dermal label precautionary statements are required for this formulation.

21-Day Rabbit Dermal - Bio-Test Lab Inc. - 1/11/73

The test material used in this study was identified as MON-2139 W.S.C.(3 lbs/gal.) Lot XHC-141.

Twenty rabbits were exposed to the level of 189.5 mg/kg/day. The test sites on half the animals were abraded. The test material was applied in an 8.2% aqueous solution at the level of 2.0 ml/kg. Length of exposure was six hours per day, five days a week.

Observations and tests for effects included mortality, reactions, body weight; hematology at day 0 and 21 included: erythrocyte, hemoglobin, hematocrit, total leukocyte count, differential leukocyte count, BUN, SAP, SGPT, and blood glucose; urine analysis, organ weights, of the brain, liver, kidney, spleen, heart, gonads, thyroid and adrenal; microscopic examination of the following tissues:

adrenal	liver	skeletal muscle
aorta	lungs	skin
brain	lymph node	small intestine
cecum	pancreas	spleen
colon siminal	parathyroid	sternum
esophagus	peripheral nerve	stomach
gall bladder	pituitary	thyroid
gonads	prostate	trachea
heart	salivary gland	urinary bladder
kidney	vesicle	uteri

Results

Nine deaths occurred among the original twenty animals between day 7 and day 15. Excitation and vocalization were noted among the animals during the second and third week of dosing.

After five applications the test material produced moderate to severe irritation. Severe irritation was noted after the tenth application (beet red erythema, severe edema, superficial escharosis, fissuring, hemorrhaging, pustules). A moderate body weight loss was observed.

A statically significant increase was noted in the total leukocyte count.

The histopathologic examination revealed twelve cases of testicular atrophy (ten moderate cases, one mild case and one slight case). Skin lesions, acanthosis, hyperkeratosis, and necrotic dermatitis were also noted.

The tests absolute weight, organ to body weight ratio and organ to brain ratio were significantly lower than the untreated control values. The no-effect level is less than 189.5 mg/kg.

21-Day Rabbit Dermal - Bio-Test Lab Inc. - 1/11/73

The test material used in this study was identified as MON-2139 W.S.C. (3 lbs/gal.), Lot No. XHC-141 and was applied as a 3.34% v/v or a 5.01% v/v in water. Twenty animals were used per level of 75.8 and 113.7 mg/kg. Length of exposure was six hours per day, five days a week. A 21-day post treatment observation period was used for ten animals.

Observations and tests for effects included mortality, reactions, body weight, food consumption, testes weight, and brain weight; microscopic examination of the following tissues:

adrenal	liver	skeletal muscle
aorta	lungs	skin
brain	lymph nodes	small intestine
cecum	pancreas	spleen
colon	parathyroid	sternum
esophagus	peripheral nerve	stomach
gall bladder	pituitary	thyroid
gonads	prostate	trachea
heart	salivary gland	urinary bladder
kidney	seminal vesicle	uteri

Results

Three unrelated deaths occurred. Fissures, hemorrhages, desquamation and pustules were observed at both test levels between the 5th and 15th application. Microscopic studies were reported in progress.

No-effect level is less than 75.8 mg/kg/day.

Human Patch Test - Shalanski Holding Co. - 1/11/73

The material tested was identified as MON-2139 and was tested as a 1:9 and 1:45 dilution on 50 subjects. A series of sixteen applications (0.9 ml), each of 24 hours duration were scheduled. The subjects were rested for two weeks between the fifteenth application and the challenge dose.

Results

No adverse effects were noted.

CONCLUSION

The various acute studies clearly show the technical material and the 3 lbs/gal. formulation to be in the slightly toxic category when judged by mortality. The outstanding toxic effect of the material is the ability to produce various degrees of tissue irritation. Since the proposed formulation (4 lbs/gal.) has the definite potential to produce severe ocular and dermal irritation, the signal word "Danger" should be utilized on the product label.

CODES

MON-0573 is N-phosphonomethyl glycine
CP-67573 is N-phosphonomethyl glycine
CP-70139 is the commercial formulation of the isopropylamine salt of the parent acid CP-67573.

Robert D. Coberly, Biologist
Toxicology Branch
Registration Division

cc:
DB
EEB
HFB
IRB
PCCritchlow
GEWhitmore
Division Reading File
Branch Reading File

RDCoberly/ccw
5/25/73