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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

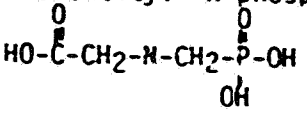
SUBJECT: Glyphosate (Roundup)-Toxicological review of the acute and subacute studies on the technical material (94-96.7%). DATE: FEB 2 1977

FROM: Toxicological

TO: Libby Zink

Petition No. 6G1679 Monsanto Agricultural Products Co.
6H5106

Chemical Identity: N-phosphonomethylglycine



Proposed temporary tolerance amendment

Former proposed		Amended increase proposed	
Crop group: citrus, cucurbits forage grasses, forage legumes, fruiting vegetables, nuts, pome fruits, root crop vegetables, seed and pod vegetables, small fruits, stone fruits and stored commodities	0.05 ppm	Crop group: citrus, cucurbits, forage grasses, forage legumes, fruiting vegetables, grain crops, leafy vegetables, ~~seed and pod~~ nuts, pome fruit: root crop vegetables, seed and pod vegetables, small fruits, stone fruits and individual commodities, avocado, cotton seed, hops and sugarcane.	0.1 ppm
Fish	0.15	Fish	2.0 ppm
		Liver and kidney of cattle, goats, hogs, horses, poultry and sheep	0.5 ppm
Temporary food additive Water (potable)	0.05 ppm	Water (potable)	0.1 ppm

Related Petitions: 4G1444, 5G1523, 5F1536, 5G1561, 6F1733/6H5116, 6G1734/6H5118, 6G1757, 6F1758/6H5126, 6F1798 6E1809, 6G1826/6H5140, 6H5144, 6F1861, 6G1862, 7G1893/7H5158

Recommendations: Toxicology Branch finds the toxicity data in file supports the proposed temporary tolernaces and food additive tolerances requested with this petition. However, T. B. concurs with Chemistry Branch recommendation of November 12, 1976 for the characterization of glyphosate residues in fish before permanent tolerances are granted. The fish restriction should remain on the label until the residues of glyphosate in fish are identified.

EPA Form 1320-6 (Rev. 6-72)

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Toxicologic review of 6G1679

Species	Route	Exposure	Formulation	Dose	Observations
Rat	Subcutaneous	acute	Tech in corn oil	>5,010	Decreased appetite and activity
Rat	Inhalation	aerosol 6 hr.	Tech.	LC_{50} > 8 mg/L	No untoward reactions
Rat	Intrapeut-oneal	acute	Tech in corn oil	470(410-540)	Decreased appetite and activity. Increased weakness and slight tremors [illegible]. Hemorrhagic lungs. Liver, kidneys and spleen dark, GI inflammation at death in 3 to 7 days.
Rat	Oral	Acute ChE activity	Tech in corn oil	5,000 10,000	No cholinesterase inhibition of plasma, erythrocytes or brain.
Rabbit	Eye	Irritation	Tech		Score 18.4 at 24 hr severe erythema slight to moderate edema and corneal dullness 10/80 all cleared by 7th day
Rabbit	Oral	21 day	Tech	0,6,18 and 60 mg/kg	NEL 60 mg/kg
Hen	Oral	Neuro-toxicity	Tech	1.25 gm/kg bid for 3 days, repeated on 21st day for a total dose of 15 gm/kg.	No signs of neurotoxicity or mortality. Histopath - no lesions to brain, spinal cord.

Subacute oral - 21 days
Method:
The technical material (96.7%) was administered in gelation capsules orally to ten young adult rabbits per level at 0,6,18 and 60 mg/kg daily for 21 consecutive days. The animals were weighted at 0, 7, 14 and 21 days. Clinical studies on blood and urine were made initially and at 21 days. The hematologic studies include differential, total leukocyte and erythrocyte count, hemoglobin concentration and hematocuit. The clinical blood chemistry studies include: fasting blood glucose concentration, BUN, SAP, SGPT, and SGOT. Urine analysis included: glucose, albumin, microscopic pH and specific gravity. Organ to body weights of each rabbit were determined in the following tissues: brain, liver, kidneys, spleen, heart, testes, thyroid and adrenal glands. Microscopic pathologic examinations were made on the following tissues of each

rabbit: adrenals, aorta, bone marrow, brain, caecum, colon, esophagus eyes, gall bladder, gonads, heart, kidnesy, liver, lung, lymph nodes, optic nerve, pancreas, parathyroid, sciatic nerve, pituitary, prostate, salivary glands, seminal vesicle, skeletal muscle, skin, small intestine (duodenum, jejunum and ilecum), spleen, sternum, stomach, thyroid, trachea, urinary bladder and uterus.

Results: No animals died and no unusual behavioral or systemic reaction were observed from oral administration of glyphosate for 21 days. No significant toxicologic effects were observed with any of the parameter investigated.

The following studies were reviewed in conjunction with PP No. 461444 and 5F1536.

Species	Route	Exposure	Formulation	Dose	Observations
Dog	Feeding	90 days	Tech	0,200,600, and 2,000 ppm	'NEL' > 2,000 ppm
Rat	Feeding	90 days	Tech	0,200,600, and 2,000 ppm	'NEL' > 2,000 ppm
Mouse	Carcinogenic Feeding	18 month	Tech	0,100,300 ppm	Not tumorigenic or carcinogenic at 300 ppm
Rat	Reproduction feeding		Tech	0,30,100, 300 ppm	'NEL' 100 ppm
Mouse	Mutagenic (dominant lethal)		Tech	5 and 10 mg/kg	No mutagenic at 10 mg/kg
Rabbit	Teratogenic (day 6-18 gestation)		Tech	10 and 30 mg/kg	Not teratogenic at 30 mg/kg
Rat	Feeding	2 years	Tech	0,30,100 and 300 ppm	'Nel' 100 ppm
Dog	Feeding	2 years	Tech	0,30,100 and 300 ppm	'NEL' > 300 ppm

Raymond E. Landolt

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Toxicology Branch
Registration Division

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