D-7670 / Linuron SR 8-12-81

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

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OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

AUG 12 1981

MEMORANDUM

DATE: July 16, 1981

SUBJECT: PP#1E2486. Linuron in Lettuce, (Lorox 50 WP). EPA Reg. #352-270; Minor Use Tolerance of 0.25 ppm. CASWELL#528 Accession#099948

FROM: Amal Mahfouz, Toxicologist
Toxicology Branch/HED (TS-769) Amal Mahfouz 7/16/81

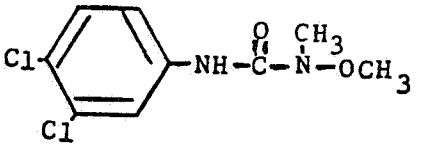
TO: Minor Use Officer
Registration Division (TS-767) WDD for LDC 7/17/81

THRU: Chris Chaisson, Acting Chief
Toxicology Branch/HED (TS-769) H for WJB

Petitioner: IR-4 National Director, Dr. R.H. Kupelian on behalf of the IR-4 Technical Committee and the Agricultural Experiment Stations Florida and Wisconsin.

Registrant: DuPont

Chemical Structure:



3-(3,4-dichlorophenyl)-1-methoxy-1-methylurea

Synonyms: Linuron, Afalon, Griffin Linex 4L, Hoe 2810, Linurex, Lorox, Premalin (discontinued), Sarlex.

Action Requested:

The petitioner requested the establishment of a tolerance for the residues of the herbicide linuron (3-(3,4-dichlorophenyl)-1 methoxy-1-methylurea) in or on lettuce at 0.25 ppm. The formulation designated for this minor use is Lorox (50% WP).

Recommendation:

Toxicology Branch recommends against the establishment of the proposed tolerance. Linuron residues of 0.25 ppm in or on lettuce would increase the existing TMRC by 1.5117%. This increase is above the 1% level allowed by the 9/30/80 Minor Uses Policy. The herbicide is under regulatory action at the present time as a pre-RPAR due to an oncogenic trigger.

Mutagenicity studies should be provided in support of future tolerances.

Related Petitions and Tolerances:

Related Petitions: PP#356, #413, #7F0542, #1E1148, #3E1373, 6E1767, 6G1791/H5135.

Existing Tolerances: 40 CFR 180.184; 21 CFR 561.265
Tolerances for linuron residues in or on variety of commodities are established at levels of 0.25 - 1.0 ppm

Detailed Considerations

Formulation:

Lorox is a wettable powder formulation which contains 50% by weight Linuron technical (95% minimum a.i.). All inerts are cleared under 180.1001

Use Proposed:

Lorox is to be used for selective control of broad leaf and grass weeds in lettuce. The formulation is to be used as a single application (ground spray) 2 weeks after germination at a rate of 0.5 lb a.i./A (1 lb Lorox). PHI is 35 days.

Lorox should be used only East of Mississippi River on lettuce grown on muck or peat soils only. Crops other than celery, carrots or lettuce should not be replanted within 4 months after application as injury to subsequent crops may result.

Toxicity Data:

Toxicity Data for Linuron (Technical) have been reviewed by L.B. Dale (12/12/68, including 2-year feeding in dog), C. Frick (12/10/79, one teratology study in rat), and W. Dykstra (5/6/80, a 2-year feeding in rat). The presence of an additional teratology study on rabbit was noted in a 12/11/78 memo by R. Engler. Acute studies on Lorox 50% WP were not available.

The above mentioned reviews reflected the following NOELs:

°Teratology - Rat	NOEL = 125 ppm
°3-Generation Reproduction - Rat	NOEL = 125 ppm
°Two-Year Chronic Feeding - Rat	NOEL = 125 ppm
°Two-Year Chronic Feeding/Oncogenic - Rat	Positive oncogen
°Two-Year Chronic Feeding - Dog	NOEL = 25 ppm

The Allowable Daily Intake (ADI) of Linuron is 0.0063 mg/kg/day based on the two-year dog feeding NOEL of 25.0 ppm and a 100 fold safety factor. The Maximum Permissible Intake (MPI) is 0.3750 mg/kg/60 kg man. The Theoretical Maximal Residues Contribution (TMRC) calculated from the existing tolerances is 0.3248 mg/kg/day/1.5 kg diet or 86.61% of the MPI.

The proposed residues of 0.25 ppm in or on lettuce would increase the TMRC by 0.00491 mg/kg/1.5 kg diet or 1.5117% (see attached Printout).

Linuron is an oncogen causing a dose-related increases of benign testicular interestial cell adenomas in male rats fed 125 and 625 ppm. The chemical has been referred to the Special Pesticide Review Division (SPRD) for pre-RPAR review (4/7/80 memo by W. Dykstra).

The OPP Policy on Minor Uses (9/30/80) for pre-RPAR chemicals allows the establishment of new tolerances for minor uses when the incremental residues concentration of the proposed use is 1% or less of the existing TMRC. The proposed tolerance of 0.25 ppm in or on lettuce is higher than the 1% value permitted by the Minor Uses Policy and consequently cannot be supported.

No new toxicity data were submitted. All data considered for this action are summarized in the attached toxicity table.

Data Gaps:

No mutagenicity studies are available on this technical product.

Attachment

Toxicity Summary (Technical)

Study	% a.i.	Results	Core Classification
Acute Oral - Rat	95	LD_{50} 2.1 g/kg	Not Core graded
90-Day Feeding - Rat	95	NOEL = 80 ppm LEL = 400 ppm	Not Core graded
2-Year Chronic Feeding - Rat	95	NOEL = 125 ppm	Not Core graded
2-Year Chronic Feeding - Dog	95	NOEL = 25 ppm Dose-related abnormal blood pigment at feeding levels of 25, 125 and 625 ppm; weight loss at highest dose level (625 ppm)	Not Core graded
3-Generation Reproduction -	95	NOEL = 125 ppm	Not Core graded
Eye Irritation - Rabbit	95	0.1 ml of 10% suspension - no effect	Not Core graded
Skin Irritation - Guinea - Pig	95	10% aqueous suspension of 50% WP caused moderate irritation, no sensitization.	Not Core graded
Teratology (feeding) - Rabbit	95	NOEL = 125 ppm	
Teratology - Rat Haskell Lab.#33-79	97	NOEL = 125 ppm LEL = 625 ppm (resportion)	Guideline
2-Year Chronic Feeding - Rat Haskell Lab.#100-80	97	Oncogenic: dose-related increase in benign testicular interestitial cell adenoma in males at 125 and 625 ppm; also reticulocytosis in females at all levels, 50, 125 and 625 ppm as reflected by lower RBC counts and low hemoglobin and hematocrit.	Minimum