D-7649 / Linuron 3-8-85

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

Releasable

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Linuron on Carrots, Calculation of Mixer/Loader and Pilot Systemic Dose from Dermal Exposure and Dermal Absorption and Calculation of Oncogenic Risk Assesment

TO: Robert Taylor PM-25
Registration Division (TS-767)

FROM: Robert P. Zendzian PhD, Acting head 3/8/85
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and

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HED (TS-769)

Compound Linuron

Tox Chem #528

Registration #352-326

Registrant duPont

Action Requested

A) Determine systemic dose of mixer-loaders and pilots exposed to linuron during application to carrots from exposure data provided by Curt Lunchick Chemist (Memo 3/6/85)

B) Perform an oncogenic risk assesment for linuron exposure of mixer-loaders and pilots.

Conclusion

A) The maximum annualized systemic dose has been calculated for the following conditions as;

I. Florida
a) Mixer-Loader, exposure 150 X 10^{-3}mg/kg/day.
Two hours per day for a total dermal dose of 6.4 mg/kg/year

Systemic dose = 0.9 X 10^{-3}mg/kg/day

b) Pilot, exposure 7 X 10^{-3}mg/kg/day.
Two hours per day for a total dermal dose of 0.29mg/kg/year

Systemic dose = 0.04 X 10^{-3}mg/kg/day

II. Kern County
a) Mixer-Loader, exposure 460 X 10^{-3}mg/kg/day.
Two hours per day for a total dermal dose of 21.0 mg/kg/year

Systemic dose = 3.0 X 10^{-3}mg/kg/day

b) Pilot, exposure 14 X 10^{-3}mg/kg/day.
Two hours per day for a total dermal dose of 0.63mg/kg/year

Systemic dose = 0.09 X 10^{-3}mg/kg/day

B. The oncogenic risk asssemant has been calcualted for the following conditions as;

I. Florida
a) Mixer-Loader, Risk = 1.3 X 10^{-4}

b) Pilot, Risk = 6.6 X 10^{-6}

II. Kern County
a) Mixer-Loader, Risk = 4.3 X 10^{-4}

b) Pilot, Risk = 1.3 X 10^{-5}

Discussion

Data on the dermal exposure to linuron during field use has been provided by Curt Lunchick of EAB as follows (Memo 3/6/85).

I, Florida
a) Mixer-Loader, exposure 150 X 10^{-3}mg/kg/day.
Two hours per day for a total true dose of 6.4 mg/kg/year

b) Pilot, exposure 7 X 10^{-3}mg/kg/day.
Two hours per day for a total true dose of 0.29mg/kg/year

II, Kern County
a) Mixer-Loader, exposure 460 X 10^{-3}mg/kg/day.
Two hours per day for a total true dose of 21.0 mg/kg/year
b) Pilot, exposure 14 X 10^{-3}mg/kg/day.
Two hours per day for a total true dose of 0.63mg/kg/year

The appropriate rate of absorption will be taken from the results of the rat dermal absorption study submitted by the Registrant, du Pont. The values utilized are taken from Table D from the DER.

Table D. Percentage of applied radioactivity absorbed as a function of time corrected for outlying values. Total of blood, urine and feces. (mean of 4 animals)

Time (hours)	0.5	1.0	2.0	4.0	10
Dose mg (Female,Male)					
0.12 F	0.8	2.1[a]	3.4	6.2	13.9
0.12 M	0.7	2.7	5.3	9.0	18.1
1.00 M	0.2	0.3[b]	2.1	2.8	16.4
7.4 M	<0.1	0.1	0.7	1.5	2.5

a.mean of 3 urine and 3 fecal values
b.mean of 2 urine and 3 fecal values

Only the values for male animals will be used. The doses listed in the table are each applied to the same area of skin on the individual rats (4 in^2). It will be noted that for each time interval the percentage of the dose absorbed decreases (the quantity absorbed increases up to the limit imposed by the nature of the compound and the permiability of the skin). thus it is necessary to select to percent absorption from the dose to the rat which most closely approximates the dose, per 4 in^2, that is received by to workers. The exposed skin on the workers is considered to be 260 in^2.

I, Florida
a) Mixer-Loader, exposure 150 X 10^{-3}mg/kg/day is equilivant to 161 X 10^{-3}mg/4in^2.

b) Pilot, exposure 7 X 10^{-3}mg/kg/day is equilivant to 7.5 X 10^{-3}mg/4in^2.

II, Kern County

a) Mixer-Loader, exposure 460 X 10^{-3}mg/kg/day is equilivant to 625 X 10^{-3}mg/4in^2.

b) Pilot, exposure 14 X 10^{-3}mg/kg/day is equilivant to 15 X 10^{-3}mg/4in^2.

The nearest dose in the rat study to the human exposure is 0.12mg/4in^2 and the absorption values for this dose will be used.

Time (hours)	0.5	1.0	2.0	4.0	10
Dose mg					
0.12 M	0.7	2.7	5.3	9.0	18.1

For both the mixer-loaders and the pilots the absorption rate for 2 hours (5.3) will be used. These rates assume that the full dose of linuron is placed on the skin at the beginning of the exposure period to be absorbed for the whole 2 hour. This assumption over estimates the dose.

Although it has not been entered into these calculations, the rat skin is usually considered to be five times more premeable to foreign componds than the human skin. Thus the human dose can be considered as one/fifth that calculated in this document.

The Q_1* (0.33mg/kg/$^{-1}$) for oncogenic risk was obtained from the results of a lifetime feeding study in rats. A dose-related increase in testicular tumors was observed in this study.

Appendicies

Appendix I Calculations of Linuron systemic dose from dermal exposure via dermal absorption

I, Florida

a) Mixer-Loader, exposure 150 X 10^{-3}mg/kg/day.
Two hours per day for a total true dose of 6.4 mg/kg/year

5.3% absorbed per 2 hours

0.39 mg/kg/year

/365 days

0.9 X 10^{-3}mg/kg/day

b) Pilot, exposure 7 X 10^{-3}mg/kg/day.
Two hours per day for a total true dose of 0.29mg/kg/year

5.3% absorbed per 2 hours

0.02 mg/kg/year

/365

0.04 X 10^{-3}mg/kg/day

II, Kern County

a) Mixer-Loader, exposure 460 X 10^{-3}mg/kg/day.
Two hours per day for a total true dose of 21.0 mg/kg/year

5.3% absorbed per 2 hours

1.11 mg/kg/year

/365

3.0 X 10^{-3}mg/kg/day

b) Pilot, exposure 14 X 10^{-3}mg/kg/day.
Two hours per day for a total true dose of 0.63mg/kg/year

5.3% absorbed per 2 hours

0.03 mg/kg/year

/365

0.09 X 10^{-3}mg/kg/day

Appendix II; Risk Assesments

The lifetime daily dose is obtained by taking the linuron annulized mg/kg/day dose times 30/70. The lifetime risk is obtained by multiplying the lifetime dose by the Q_1^* ($0.33 mg/kg/^{-1}$).

I. Florida

a. Mixer-loader

$.9 \times 10^{-3} \times 30/70 = 0.39 \times 10^{-3}$ mg/kg/day lifetime

Risk = $.39 \times 10^{-3} \times (0.33)$

= $.13 \times 10^{-3}$

= 1.3×10^{-4}

b. Pilot

$.04 \times 10^{-3} \times 30/70 = .02 \times 10^{-3}$ mg/kg/day lifetime

Risk = $.02 \times 10^{-3} \times (0.33)$

= 6.6×10^{-6}

II. Kern County

a. Mixer-loader

$3.0 \times 10^{-3} \times 30/70 = 1.3 \times 10^{-3}$ mg/kg/day lifetime

Risk = $1.3 \times 10^{-3} \times (0.33)$

= 0.43×10^{-3}

= 4.3×10^{-4}

b. Pilot

$0.09 \times 10^{-3} \times 30/70 = 0.04 \times 10^{-3}$ mg/kg/day lifetime

Risk = $0.04 \times 10^{-3} \times (0.33)$

= 0.013×10^{-3}

= 1.3×10^{-5}