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

JUL 13 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCESMEMORANDUM

SUBJECT: O-(6-chloro-3-phenyl-4-pyridazinyl)-S-octyl-carbothioate (Pyridate Technical): Review of a study submitted by the registrant on the carcinogenicity (83-2) of Pyridate Technical in mice.

Caswell No.: 716A
HED Project No.: 2-1171
MRID Nos: 421680-01

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6-26-92

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THRU: Yiannakis M. Ioannou, Ph.D., Section Head
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and

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7/7/92

REGISTRANT: Agrolinz, Inc.

ACTION REQUESTED: To support application for registration of Pyridate containing products, evaluate the study conducted on Pyridate Technical to determine its potential carcinogenicity in mice according to FIFRA guidelines (83-2).



CONCLUSIONS:

Carcinogenicity Study in Mice (83-2) (MRID # 421680-01):

Mice (B6C3F1) were fed pyridate for 18 months at 0, 400, 800, 1600 and 7000 ppm; doses were equivalent, respectively, to 47.7, 97.1, 169.5, and 882.6 mg/kg/day in males, and to 54.5, 114.6, 204.3, and 1044.6 mg/kg/day in females. No statistically significant increases in tumor incidence relative to controls were observed in either sex at any dose, including the limit dose of 1000 mg/kg/day. Although toxicity was predominantly observed in mice treated at the highest dose, neither a NOEL nor a LOEL could be set because decrements in cumulative body-weight gains occurred in both males and females at all doses.

This study satisfies the guideline requirements (83-2) for a carcinogenicity study in mice. Classification: core minimum.

Toxicology Profile for Pyridate Technical.

A. Data Requirements (40 CFR 158.340):

<u>Data Requirements</u>	<u>Required</u>	<u>Satisfied</u>
81-1 Acute oral	yes	yes
81-2 Acute dermal	yes	yes
81-3 Acute inhalation	yes	yes
81-4 Primary eye irritation	yes	yes
81-5 Primary dermal irritation	yes	yes
81-6 Dermal sensitization	yes	yes
82-1 Subchronic feeding (rats)	yes	yes
82-1 Subchronic feeding (dog)	yes	yes
82-2 21-Day dermal	yes	yes
82-3 90-Day dermal	no	n/a
82-4 Subchronic inhalation	no	n/a
82-5 21-Day delayed neurotoxicity	no	n/a
83-1 Chronic feeding (rodent)	yes	yes
83-1 Chronic feeding (nonrodent)	yes	yes
83-2 Carcinogenicity (rat)	yes	yes
83-2 Carcinogenicity (mouse)	yes	yes
83-3 Developmental toxicity (rat)	yes	yes
83-3 Developmental toxicity (rabbit)	yes	yes
83-4 Multigeneration reproduction (rat)	yes	yes
84-2(a) Mutagenicity	yes	yes
84-2(b) Mutagenicity	yes	yes
84-4 Mutagenicity	yes	yes
85-1 Metabolism	yes	yes
85-2 Domestic animal safety	no	n/a
85-3 Dermal absorption	no	n/a

B. Toxicology Issues:

1. RfD

The current oral RfD for pyridate is set at 0.11 mg/kg/day. The critical study used in developing this value was a 2-year chronic toxicity/carcinogenicity study in rats with a NOEL of 10.8 mg/kg/day (216 ppm). A safety factor of 100 was used in determining the RfD for pyridate.

2. Data Gaps

No data gaps exist in the toxicology data base for pyridate.

C. Updated, Selected One-Liners:

Attached is an updated, selected one-liner to support the data requirements for pyridate.

