

US EPA ARCHIVE DOCUMENT



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

JUL 8 1981

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: July 2, 1981

Casual # 900A

SUBJECT: PP#OF2413/OH5275; Thio dicarb (Larvin) in/on Cotton and Soybeans; Addendum to memo of 6/10/81.

FROM: William Dykstra, Toxicologist
Toxicology Branch/HED (TS-769)

WHD for LOC 7/2/81

TO: Jay Ellenberger (12)
Registration Division (TS-767)

Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

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THRU: William Burnam, Deputy Chief
Toxicology Branch/HED (TS-769)

Recommendations:

The journal article entitled "Prevention by Arginine Glutamate of the Carcinogenicity of Acetamide in Rats", Weisburger et al. Toxicol. Appl. Pharmacol. 14, 163-175 (1969), has been reviewed and used for an oncogenic one-hit risk assessment as shown below:

Dietary levels of 2.5% acetamide to male Wistar rats for periods up to 15 months produced the following results for liver tumors:

<u>Dose</u> - 0 mg/kg/day	1250 mg/kg/day
<u>Response</u> - 0/11	12/24
<u>Incidence</u> - 0	0.5

In the June 10, 1981 memo, the rat to human conversion factor used was not fully elucidated.

The average daily dose for the rat is 1250 mg/kg/day

The equivalent human dose is $1250 \times \sqrt[3]{\frac{.40}{70}} = 223.2 \text{ mg/kg/day}$ assuming that the body weight of the average rat is 0.40 kg and the average human body weight is 70 kg. The value $\sqrt[3]{\frac{.40}{70}}$ is a factor converting the effective dose from rats to humans assuming that the amount of direct acting agent is proportional to the body surface. (Note $\sqrt[3]{\frac{.40}{70}} = \frac{1}{5.6}$)

Using Abbott's Correction, P,

$$P = \frac{0.5-0}{1-0} = 0.5$$

$$B = \frac{1}{\text{dose}} \times \ln \left(\frac{1}{1-P} \right)$$

$$B = \frac{1}{223.2 \text{ mg/kg/day}} \times \ln \left(\frac{1}{1-0.5} \right)$$

$$B = .00310 \text{ mg/kg/day}^{-1}$$

Risk = B x dietary exposure

$$\text{Risk} = 3.10 \times 10^{-3} \text{ mg/kg/day}^{-1} \times 2.263 \times 10^{-5} \text{ mg/kg/day}$$

$$\text{Risk} = 7.0153 \times 10^{-8}$$

As Toxicology Branch previously concluded the calculated risk is considered to be within the limits of acceptability and recommends that the residues of acetamide in the commodities found not require further regulation or inclusion in the tolerance of Thiodicarb.

The above risk of 7.0153×10^{-8} supercedes the risk calculated in the June 10, 1981 memo of 8.78×10^{-8} .

Also attached is the tumor data examined by Toxicology Branch's statistician using the Brown one-hit model taken from the computer terminal.

Attachment

GROUPS INCLUDED.....
LIV TUMORS
MAXIMUM DOSE LEVEL..... 1250.00

ESTIMATE OF SLOPE: 0.0005545177
ESTIMATES OF SPONTANEOUS RATES: 0.00000

WHD
Memo 6/10/81
Estimate of slope x 7 = .00388 mg/kg/day
WHD
Memo 7/2/81
Estimate of slope x 5.6 = .00310 mg/kg/day

CHI-SQUARE= 2.7060000000

UPPER CONFIDENCE BOUND ON ONEHT PARAMETERK: 0.000871

LOWER CONFIDENCE BOUND FOR DOSE ASSOCIATED WITH AN ATTRIBUTABLE RISK:

LOWER BOUND:	.1148D-04	AT RISK	.1000D-07
LOWER BOUND:	.1148D-03	AT RISK	.1000D-06
LOWER BOUND:	.1148D-02	AT RISK	.1000D-05
LOWER BOUND:	.1148D-01	AT RISK	.1000D-04
LOWER BOUND:	.1148	AT RISK	.1000D-03
LOWER BOUND:	1.149	AT RISK	.1000D-02

CHI-SQUARE= 5.4118900000

UPPER CONFIDENCE BOUND ON ONEHT PARAMETERK: 0.001032

LOWER CONFIDENCE BOUND FOR DOSE ASSOCIATED WITH AN ATTRIBUTABLE RISK:

LOWER BOUND:	.9692D-05	AT RISK	.1000D-07
LOWER BOUND:	.9692D-04	AT RISK	.1000D-06
LOWER BOUND:	.9692D-03	AT RISK	.1000D-05
LOWER BOUND:	.9692D-02	AT RISK	.1000D-04
LOWER BOUND:	.9692D-01	AT RISK	.1000D-03
LOWER BOUND:	.9697	AT RISK	.1000D-02

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THE BROWN ONE-HIT MODEL

D A T A T O B E A N A L Y Z E D
(NUMBER RESPONDERS / NUMBER AT RISK)

EXPERIMENTAL GROUPS.....

DOSE	LIV TUMORS
0.0	0/11
1250.000	12/24

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