JUL 8 1981

MEMORANDUM

DATE: July 2, 1981

Caswell # 900 A

SUBJECT: PP#0F2413/0H5275; Thiodicarb (Larvin) in/on Cotton and
          Soybeans; Addendum to memo of 6/10/81.

FROM: William Dykstra, Toxicologist   *WHD for LDC 7/2/81*
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TO: Jay Ellenberger (12)
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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:

Dose - 0 mg/kg/day	1250 mg/kg/day
Response - 0/11	12/24
Incidence - 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 $1250 \times \sqrt[3]{\frac{.40}{70}} = 223.2$ 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 effetive 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,

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

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

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

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

Risk = B x dietary exposure

Risk = 3.10×10^{-3} mg/kg/day^{-1} x 2.263×10^{-5} mg/kg/day

Risk = 7.0153×10^{-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

CHI-SQUARE=   2.7060000000
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UPPER CONFIDENCE BOUND ON ONEHIT 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
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UPPER CONFIDENCE BOUND ON ONEHIT 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

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