

UNDATED

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NOTE TO CHRIS CHAISSON

re: Thiodicarb/Acetamide Risk
Calculation for Sweet Corn

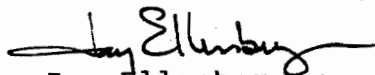
Attached is a copy of RCB's review of Union Carbide's residue levels of acetamide from the cow study. As you recall you, Bill Burnam and I discussed a few weeks ago that after RCB verified the residue data your group would write me a brief memo concurring with Union Carbide's figures for the risk calculation. This is needed so that we can proceed with the sweet corn tolerance.

Note my comment at the bottom of RCB's review. I've talked to Bob Quick about this. He did not have any problems with Carbide's correction, however the RCB review was completed before he received a copy of the correction.

Using the corrected residue figure for the 10 ppm feeding level, the correct ratio of thiodicarb to acetamide is 306. This will then give a calculated risk level of 7×10^{-9} .

I've attached copies of the original Carbide data submitted to RCB and to Tox for review, the expedited memo from Camp to Melone and RCB's review. Also, I've attached a copy of my risk calculations.

Please provide me with the Tox. memo by this Friday.


Jay Ellenberger
Registration Division

EPA Correspondence No. 180-83
June 16, 1983

U.S. ENVIRONMENTAL PROTECTION AGENCY
Registration Division (TS-767C)
Insecticide/Rodenticide Branch
Crystal Mall Building 2 - Room 202
1921 Jefferson Davis
Arlington, Virginia 22202

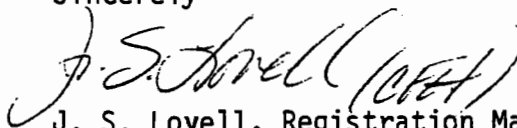
Attn: Jay S. Ellenberger
Product Manager (12)

Re: Transfer of Thiodicarb levels in the diet of cows to acetamide in
tissues and milk.

Dear Mr. Ellenberger:

Confirming our previous conversations on this topic (the last of which was on June 15, 1983) we have discovered a typographical error in "Studies On The Disposition of ^{14}C Thiodicarb in Lactating Cows." This was submitted to the Agency in September of 1980 as a part of our petition for tolerances in/on cotton and soybeans. Table 8 of that study presents the resulting levels of various Thiodicarb metabolites in the tissues and milk of cows from a 21-day continuous feeding study. The value given for acetamide in cow liver tissue at the 10 ppm feeding level is shown as 0.143 ppm when it is actually 0.0143 ppm. A letter from Dr. R. W. Heintzelman, group leader for Environmental Chemistry and Metabolism, confirming the error in the original document is attached.

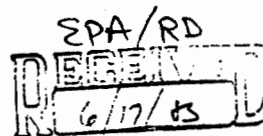
Sincerely



J. S. Lovell, Registration Manager
Insecticides and Intermediates
Registration & Regulatory Affairs

JSL/gb

Attachment: Memo/ re: Metabolism & Environmental Chemistry, R.W. Heintzelman



UNION CARBIDE AGRICULTURAL PRODUCTS COMPANY, Inc.

To Name	J.S. Lovell	Date	June 16, 1983
Division		From (Name & Dept.)	R.W. Heintzelman
Location	RTP	Answering letter date	Metabolism & Environmental Chemistry
Floor Number	2156	Subject	Thiodicarb Meat & Milk Study - Acetamide in Liver
Copy to	S.L. Harrison G.G. Madgwick R.J. Otten D.E. Thurman		

Due to the recent questions raised concerning the levels of acetamide in the tissues of cows treated with thiodicarb I have been reviewing the data on this subject. Table VIII in the report "Studies on the Disposition of ¹⁴C-Thiodicarb in Lactating Cows" by C.S. Feung, P.R. College, and E.L. Chancey shows that the level of acetamide in the liver from the various cows was as follows:

<u>Thiodicarb Treatment Level (ppm)</u>	<u>Reported Acetamide Levels (ppm)</u>
10	0.143
30	0.166
100	0.677

A review of the raw data shows that there is an error in the level of acetamide in liver reported for the 10 ppm thiodicarb feeding level. The reported level is 0.143 ppm while the actual value is ten-fold lower, ie 0.0143 ppm. The error was evidently made in writing and/or typing of the report. I understand that you have already discussed this point briefly with EPA. This letter can serve as confirmation that a mistake was, in fact, made in the original report.

RWH/sr

R. W. Heintzelman

EPA/RD
RECEIVED
6/17/83

88

21 DAY COW FEEDING STUDY (OF 2413/045275)

Thiodicarb!
1 Feeding Level

Ratio of Thiodicarb fed/da
to Level of Acetamide ~~in~~
in the Body ^Y

100 ppm 75:1

30 ppm 11.9:1

} Calculated

10 ppm 306:1

1.2 ppm ^{2/} 524:1 ^{4/}

} extrapol.

0.03 ppm ^{3/} 934:1 ^{4/}

(In hens at a 100 ppm feeding level, the ratio was 500:1)

1/ Calculated based on actual levels found in ^{the} liver, spleen, kidney, + muscle tissue and assuming the remainder of the carcass contained acetamide at the same level as in ~~the~~ muscle tissue.

2/ 1.2 ppm is the level of thiodicarb in the human diet at ~~the~~ 100% of the ADI.

3/ 0.03 ppm is the level of thiodicarb in the human diet from consumption of sweet corn containing thiodicarb

4/ residues at the tolerance level (2.0 ppm). ⁴
FROM CORN FEED TO MILK, FAT, + MEAT (Concentration Coefficient: 86)

MISSING LOW WL. - 1000 lbs

TOTAL ACETAMIDE

Residue Data taken from Cow data

TISSUE	AVERAGE WEIGHT	10 ppm		30 ppm	
		mg (ppm)	0.78	mg (ppm)	100 ppm
LIVER	5.45 Kg (1.2%)	0.076 (0.014)	0.905 (0.166)	3.69 (0.677)	
KIDNEY	1.36 Kg (0.3%)	0.067 (0.005)	0.060 (0.044)	0.083 (0.061)	
SPLLEEN	1.0 Kg (0.17%)	0.004 (0.004)	0.0170 (0.017)	0.022 (0.022)	
MUSCLE	90.9 Kg (20%)	0.046 (0.0005)	0.636 (0.007)	3.63 (0.040)	
Remainder	98.71 Kg (21.67%)	0.178	2.50 (0.007)	14.27 mg (0.040)	
<u>TOTAL ACETAMIDE ALL TISSUES</u>		<u>0.535 mg</u> 1.24	<u>(4.118 mg)</u>	<u>(21.893 mg)</u>	

If assume the remainder of the body contains the same as the muscle:

At 10 ppm level:

$$\frac{0.001 \text{ mg}}{\text{Kg}} \times 356.8 \text{ Kg} = 0.3568 \text{ mg}$$

30 ppm level

$$\frac{0.007 \text{ mg}}{\text{Kg}} \times 356.8 \text{ Kg} = 2.50 \text{ mg}$$

100 ppm level

$$\frac{0.040 \text{ mg}}{\text{Kg}} \times 356.8 \text{ Kg} = 14.27 \text{ mg}$$

∴ 16.3.6 mg TD → 0.535 mg A } 13

491 mg TD → 4.118 mg A } 11

1636 mg TD → 21.893 mg A } 9

6 → 1
356 → 159

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

cc: Dech Ma

Handwritten notes: H... RCB T... (partially illegible)

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

JUN - 6 1983

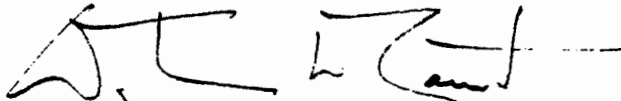
MEMORANDUM

TO: John W. Melone, Director
Hazard Evaluation Division (TS-769)

SUBJECT: Review of Thiodicarb/Acetamide Residue and
Risk Data

I request an expedited review by Toxicology and Residue Chemistry of the above action which has already been delivered to the reviewers. This review is necessary in order for us to proceed, at Ed Johnson's request, with the processing of the pending tolerance and registration for thiodicarb on sweet corn and the technical registration.

Union Carbide has provided calculations of acetamide residue levels in animal tissue from different feeding levels of the parent compound, thiodicarb. Carbide representatives presented and discussed their calculations in a recent meeting with Bill Burnam, Anne Barton and others. These calculations are to be used for calculating the oncogenic risk to humans from consuming sweet corn. Please have the appropriate reviewers from each Branch get together to review Union Carbide's calculations to determine whether they concur with them. Any questions on this can be addressed to Jay Ellenberger, Product Manager 12, at 557-2386.


Douglas D. Campt, Director
Registration Division (TS-767)

3F2773

See - 716
7



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

JUN 17 1983

EXPEDITE

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#3F2773: Thiodicarb/Acetamide Residues
and Risk Data. Submission of 5/31/83

FROM: Alfred Smith, Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

TO: Jay Ellenberger, P.M. No. 12
Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

RCB has been requested by RD (see Campt memo, 6/6/83 and Ellenberger note of 6/2/83) to comment on the correctness of cattle feeding study calculations submitted by Union Carbide. These calculations are to be used in a risk assessment and involve the ratio of thiodicarb fed to cattle to the level of acetamide found.

* The petitioner's submission has been reviewed and evaluated. The residue data taken from the cow feeding study (section D, part II of III, Study #12, Table VIII) contains one error. The total acetamide reported in liver at the 10 ppm level should be 0.143 ppm instead of the 0.014 ppm listed. The corresponding weight should be 0.78 mg acetamide instead of 0.076 mg. This change results in a total of 0.881 mg acetamide for the four organs instead of 0.178 mg. As a result, the total acetamide for all tissues is 1.238 mg instead of the listed 0.535 mg.

* The corrected ratio of Thiodicarb/acetamide for the 10 ppm level is 132 instead of 306.

We have no objection to the assumption noted in item 1 of the footnotes.

TS-769:RCB:A.Smith:mch:CM#2:Rm810:X77377:6/17/83

cc: R.F., Circu., A. Smith, Thompson, FDA, TOX, EEB, EAB,
PP#3F2773

RDI: R. Quick, 6/17/83

On 6/17/83 Union Carbide submitted a correction to the cow metabolism data, showing the correct amount of acetamide in the liver to be 0.0143 ppm, not 0.143 ppm as originally reported. This has not been considered in paragraphs 2 & 3 above. I believe the correct ratio is 306.

*