

CASE GS238

METIRAM

STUDY 6

PM

CHEM 014601

Metiram/ETU

BRANCH EAB

DISC

ACTIVE INGREDIENT-<sup>14</sup>C-Ethylene labeled ETU of 10.08 mCi/mole and 97.8% radiochemical purity.

FICHE/MASTER ID 404661-03

M. Carpenter. 1987. Hydrolysis as a function of pH at 25°C of <sup>14</sup>C-Ethylenethiourea. Unpublished study prepared by ABC laboratories for Roam and Haas and received Jan. 18, 1988 in response to the Mancozeb Registration Standard. Acc. 404661-03.

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CONCLUSION:Hydrolysis:

1. This study is acceptable and along with study 4 on metiram together satisfy EPA Hydrolysis Data Requirement on ETU and metiram for Registration.
2. No detectable degradation of ETU occurred at pH 5, 7, and 9 in 30 days. Therefore, no breakdown of ETU due to hydrolysis is expected in the environment.

MATERIALS AND METHODS:

A primary stock solution of 97.8% pure <sup>14</sup>C labeled ETU in methanol contained  $4.35 \times 10^7$  dpm/ml ( $1.94 \times 10^3$  ug/ml) was used. The following sterilized buffer solutions were prepared (water and equipment were sterilized before use):

200 ml pH 5: 14.8 ml of 0.2 M acetic acid + 35.2 ml of 0.2 M NaAc + water

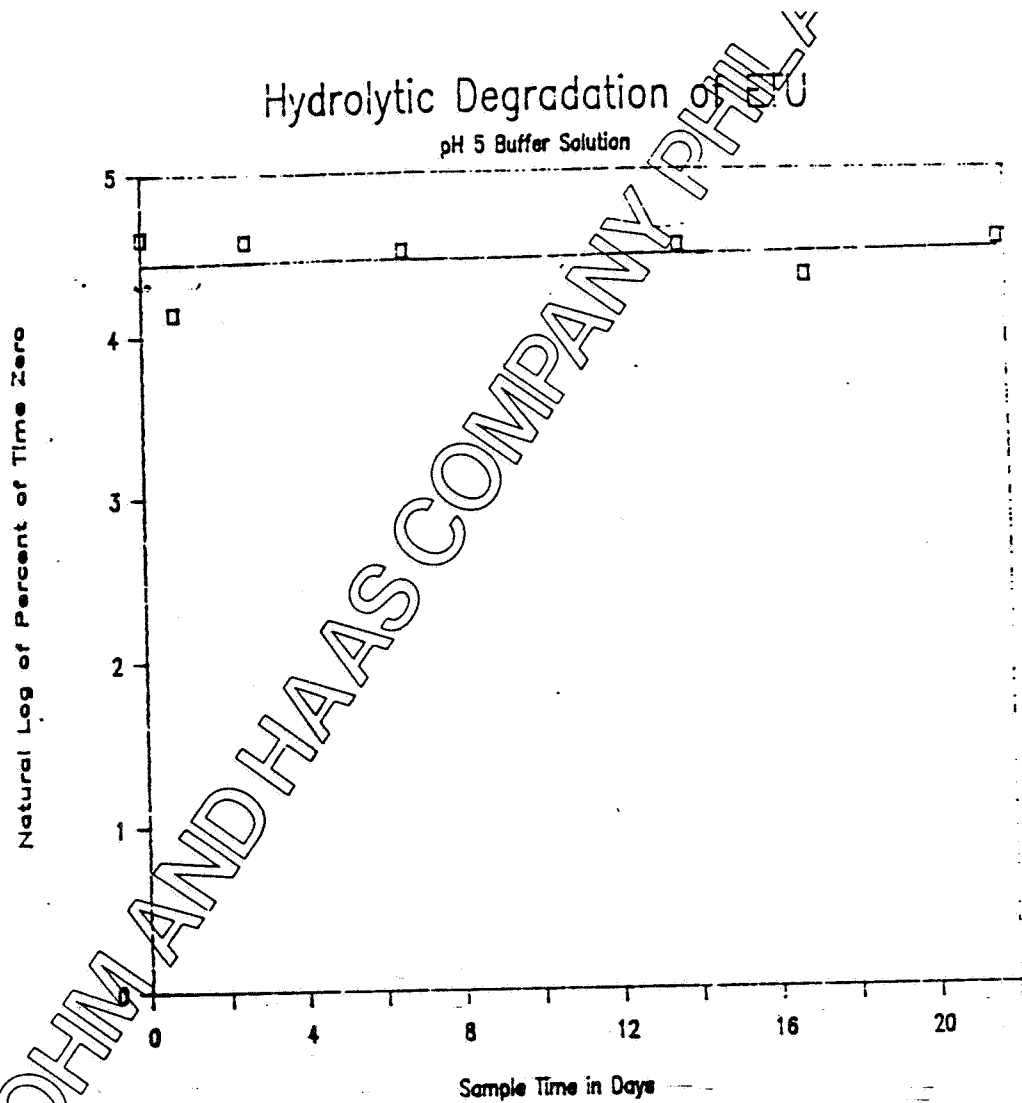
1000 ml pH 7: 22.2 ml of 0.01 M N-2-hydroxyethylpiperazine-N'-2-ethanesulfonic acid + 0.2 M KOH until a pH-7 was reached.

1500 ml pH 7: 75 ml of 0.2 M tris(hydroxymethyl)aminomethane + 70.5 ml of 0.2 M HCl + water

200 ml pH 9: 23 ml of 0.2 M boric acid + 32 ml of 0.2 M borax solution + water.

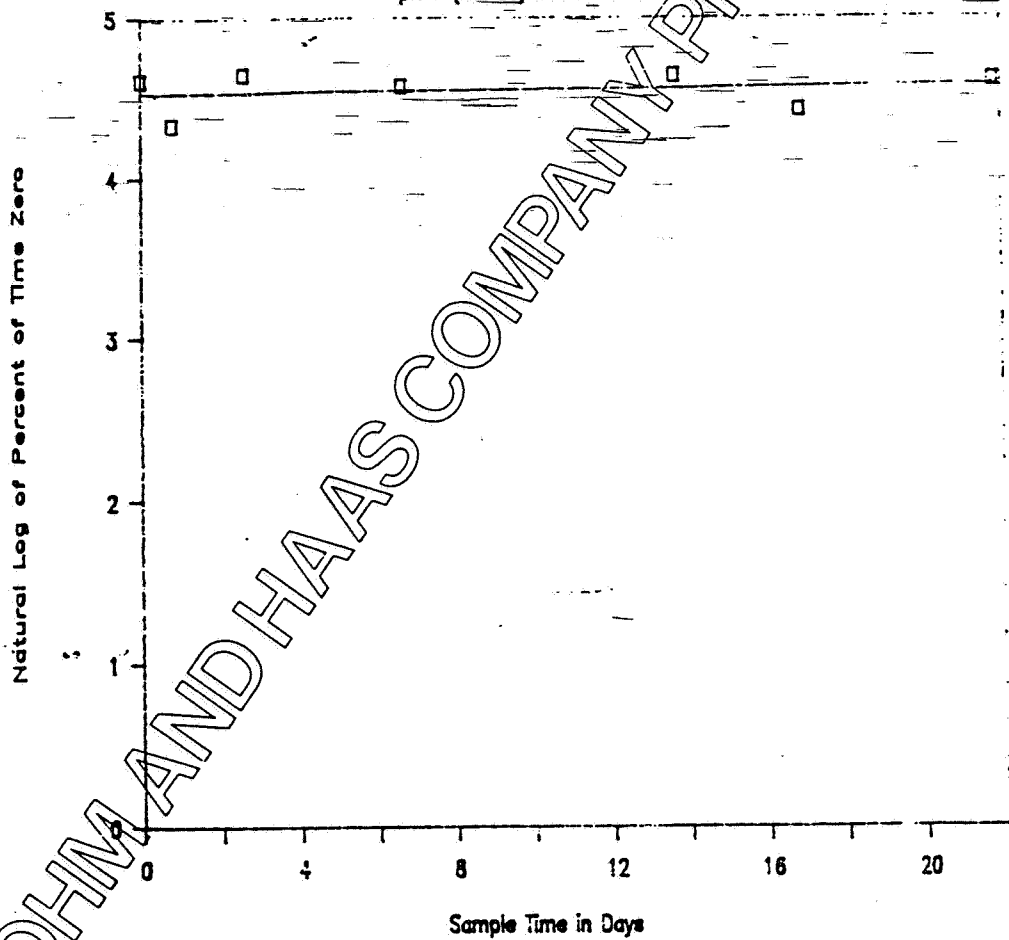
The test solutions of pH 5, 7 and 9 were prepared by adding 0.498 ml of the  $^{14}\text{C}$ -ETU stock solution to each flask, evaporating the solvent and then 100 ml of the appropriate buffer was added. Each flask was placed in a box at 25°C. Samples were taken after 0 (blank), 1, 2, 3, 7, 14, 17, 22, and 30 days and analyzed by LSC for total radioactivity and by TLC and HPLC in reference to authentic samples of parent and potential degradates.

REPORTED RESULTS:

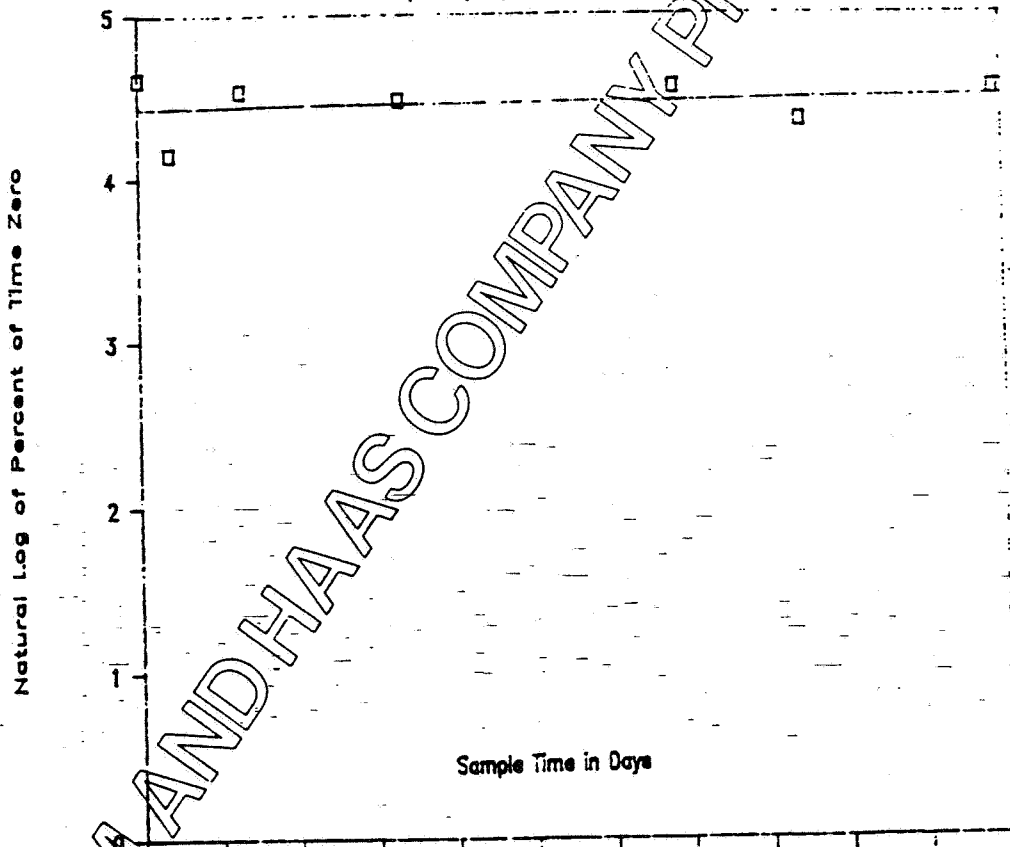


# Hydrolytic Degradation of PEG

pH 7 (HEPES) Buffer Solution

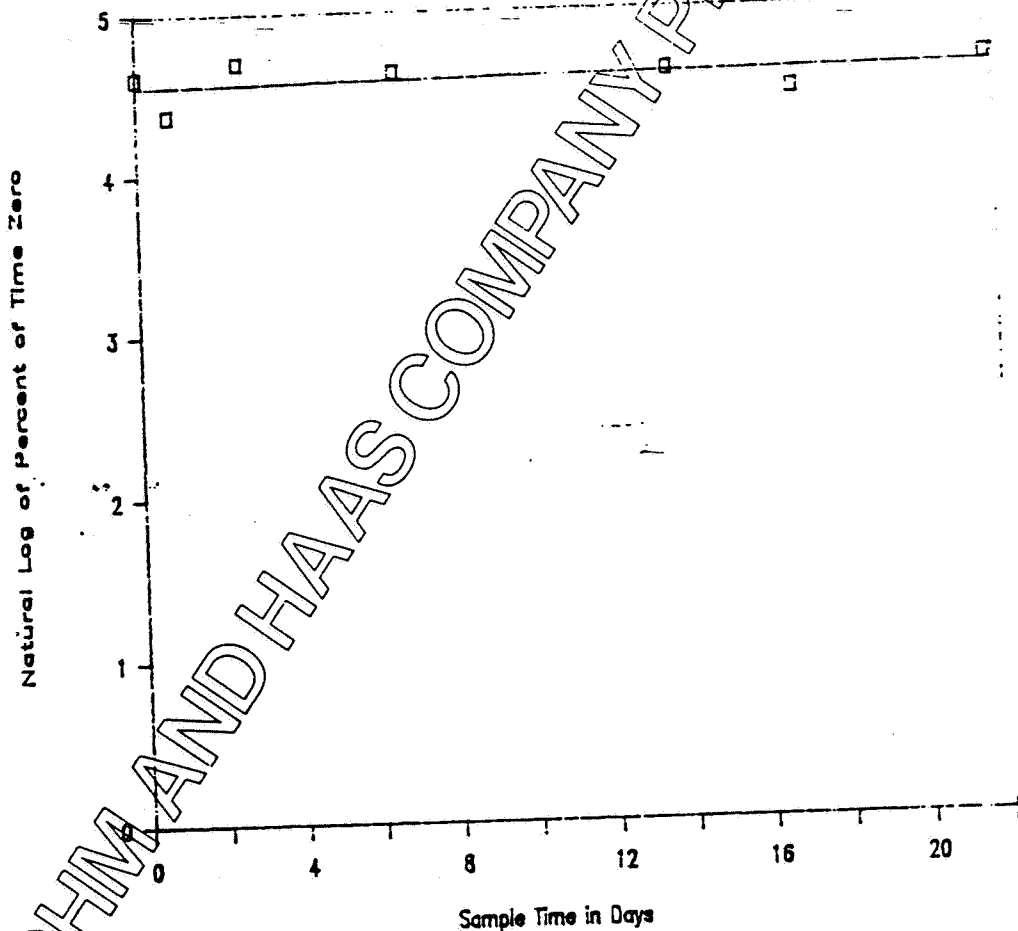


pH 7 (Tris) Buffer Solution



# Hydrolytic Degradation of $^{14}C$

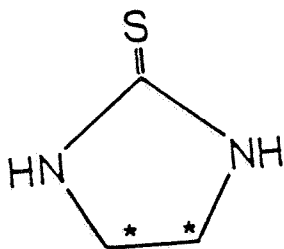
pH 9 Buffer Solution



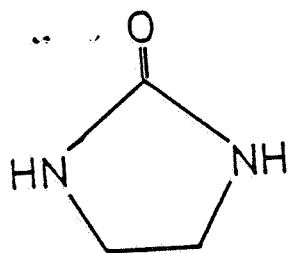
## DISCUSSION:

1. Degradation observed on the TLC plates was attributed to photodegradation due to exposure to the UV detector light and was observed with all samples of ETU.
2. Recoveries accounted for over 96.8% of the applied radioactive material.

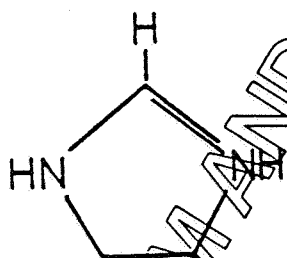
FIGURE 1  
Structure and Nomenclature of  $^{14}\text{C}$ -Ethylenethiourea  
and Expected Degradation Products



$^{14}\text{C}$ -Ethylenethiourea



Ethyleneurea

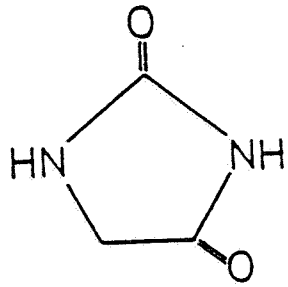


2-Imidazoline

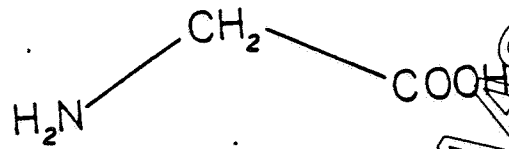
\*Denotes  $^{14}\text{C}$ -labeling.

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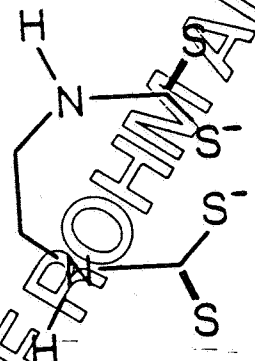
FIGURE 1 (Continued)  
Structure and Nomenclature of <sup>14</sup>C-Ethylenethiourea  
and Expected Degradation Products



Hydantoin



Glycine



Mn<sup>+2</sup> / Zn<sup>+2</sup>  
10 / 1

Ethylene bis Dithio-  
Carbamate

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TABLE II  
 Definitive Hydrolysis of <sup>14</sup>C-Ethylenethiourea in pH:5 Buffered Solution

Sample Day	µg/ml as Parent Equivalents	Z as Parent As Determined by RTLC	µg/ml as Parent Compound	pH 5 Samples		In of Percent Time Zero	Regression Output
				Percent of Time Zero	Constant Y Intercept		
0	9.04	86.0	7.71	100.0%	4.61	0.167	
0.79	8.67	56.4	4.89	63.9%	4.14	0.0321	
2.61	8.76	86.8	7.60	97.8%	4.58		
6.67	8.75	81.0	7.09	91.2%	4.51	No. of Observations	8
13.7	8.63	83.9	7.24	93.1%	4.34	Degrees of Freedom	6
16.9	8.70	68.5	5.96	76.7%	4.34	Y Coefficient(s) <sup>1</sup>	0.00260
21.8	8.70	85.3	7.42	95.5%	4.56	Std. Err. of Coef.	0.00583
29.7	9.11	78.9	7.19	92.5%	4.53		

<sup>1</sup>Positive slope indicates no significant degradation occurred. Data precludes calculation of rate constant and half-life.

TABLE III  
 Definitive Hydrolysis of <sup>14</sup>C-Ethylenethiourea in pH 7H Buffered Solution

Sample Day	pH 7H Samples										
	$\mu\text{g/ml}$ as Parent Equivalents	$\lambda$ as Parent As Determined by RTLC	$\mu\text{g/ml}$ as Parent Compound	Percent of Time Zero	ln of Percent Time Zero	Constant Y Intercept	Regression Output	Std. Err. of Y Est.	R Squared	No. of Observations	Degrees of Freedom
0	9.22	81.3	7.50	100.0%	4.61	4.53	0.124	0.0493	8	6	0.00241
10.79	8.97	63.4	5.69	75.9%	4.33						0.00432
2.62	8.98	87.4	7.85	104.7%	4.65						
6.67	8.93	81.3	7.26	96.9%	4.57						
13.7	9.02	86.3	7.78	103.8%	4.54						
16.9	9.05	68.5	6.20	82.7%	4.42						
21.8	8.74	85.8	7.50	100.0%	4.61						
29.7	9.10	83.3	7.58	101.1%	4.62						

<sup>1</sup> Positive slope indicates no significant degradation occurred. Data precludes calculation of rate constant and half-life.



TABLE IV  
 Preliminary Hydrolysis of <sup>14</sup>C-Ethylenethiourea in pH 7T Buffered Solution

Sample Day	pH 7T Samples						Regression Output
	µg/ml as Parent Equivalents	% as Parent As Determined by RFLC	µg/ml as Parent Compound	Percent of Time Zero	ln of Percent Time Zero	Constant Y Intercept	
0	9.02	91.5	8.25	100.0%	4.61	4.48	0.155
0.79	9.10	57.6	5.24	63.5%	4.15	0.0377	
2.62	8.93	85.5	7.64	92.3%	4.53		
6.67	9.03	80.2	7.24	87.1%	4.47		
13.7	9.07	86.0	7.80	94.5%	4.55		
16.9	9.19	69.2	6.36	77.1%	4.34		0.00262
21.8	8.92	85.8	7.65	92.7%	4.53		0.00541
29.7	9.21	81.4	7.50	90.8%	4.51		

! Positive slope indicates no significant degradation occurred. Data precludes calculation of rate constant and half-life.

TABLE V  
Definitive Hydrolysis of <sup>14</sup>C-Ethylenethiourea in pH 9 Buffered Solution

Sample Day	pH 9 Samples											
	µg/ml as Parent Equivalents	% as Parent As Determined by RTLC	µg/ml as Parent Compound	Percent of Time Zero	ln of Percent Time Zero	Regression Output	Constant Y Intercept	Std. Err. of Y Est.	R Squared	No. of Observations	Degrees of Freedom	Coefficient(s) <sup>1</sup>
0	9.68	73.9	7.15	100.0%	4.61	4.55	0.109	0.0991	8	6	0.00309	0.00380
0.77	9.35	60.6	5.67	79.2%	4.37							
2.61	9.33	83.1	7.75	108.4%	4.69							
6.67	9.37	77.5	7.26	101.5%	4.62							
13.7	9.40	76.5	7.19	100.5%	4.61							
16.9	9.38	67.4	6.32	88.4%	4.48							
21.8	9.25	81.7	7.56	105.6%	4.66							
29.7	9.24	81.4	7.52	105.1%	4.66							

<sup>1</sup>Positive slope indicates no significant degradation occurred. Data precludes calculation of rate constant and half-life.

TABLE VI

Mass Balance of <sup>14</sup>C-Ethylenthiourea Hydrolysis Study Samples

Sample Day	µg/ml pH 5	Percent of to pH 5	µg/ml pH 7H	Percent of to pH 7H	µg/ml pH 7T	Percent of to pH 7T	µg/ml pH 9	Percent of to pH 9
0	9.04	100.0%	9.72	100.0%	9.02	100.0%	9.68	100.0%
0.79	8.67	95.9%	8.97	97.3%	9.10	100.9%	9.35	96.6%
2.62	8.76	96.9%	8.98	97.4%	8.93	99.0%	9.33	96.4%
6.67	8.75	96.8%	8.93	96.9%	9.03	100.1%	9.37	96.8%
13.7	8.63	95.5%	9.02	97.8%	9.07	100.6%	9.40	97.1%
16.9	8.70	96.2%	9.05	98.2%	9.15	101.9%	9.38	96.9%
21.8	8.70	96.2%	8.74	94.8%	8.92	98.9%	9.25	95.6%
29.7	9.11	100.8%	9.10	98.7%	9.21	102.1%	9.24	95.5%
	Mean = 97.3%		Mean = 97.6%		Mean = 100.4%		Mean = 96.8%	

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