APPENDIX B: SYNONYMS AND TRADE NAMES OF ETU

Chemical Abstracts Service Registry Number 96-45-7 NIOSH RTECS Number NI96250 4,5-Dihydroimidazole-2(3H)-thione 4,5-Dihydro-2-mercaptoimidazole N,N'-(1,2-Ethanediy1)thiourea Ethylene thiourea 1, 3-ethylene-2-thiourea N,N'-Ethylenethiourea Imidazolidinethione Imidazoline-2-thiol Imidazoline-2(3H)-thione 2-imidazolidenethione 2-imidazolidene-2-thiol Jor 4022 Mercaptoimidazoline 2-Mercaptoimidazoline 2-Mercapto-2-imidazoline N, N'-ethylene-thiourea NA-22 NA-22DNA-22F National Bureau of Standards Standard Reference Material 392 Pennac CRA Robac 2.2 Rhodanin S-62 Sodium-22 neoprene accelerator Tetrahydro-2H-imidazole-2-thione Thiate-N 2-thiol-dihydroglyoxaline Thiourea, N, N 1 (1, 2-ethandiy1) 2H-Imidazole -2-thione, tetrahydro 4,5-Dihydro-2-mercaptoimidazole

Vulkacit NPV/C Warecure C

APPENDIX C
NIOSH ESTIMATE OF TYPES OF WORKERS EXPOSED TO ETU (Imidazolidinethione, 2-)
IN THE MANUFACTURE OF FABRICATED RUBBER PRODUCTS

National Occupational Hazard Survey (Projected) as of 3/7/78

Classification of Worker	No. of Exposures	% of Total
oldollication of worker		TOTAL
Industrial Engineers	30	0.2
Chemists	420	2.5
Personnel and Labor Relations Workers	60	0.4
Engineering and Science Technicians, N.E.C.	120	0.7
Research Workers, Not Specified	30	0.2
Managers and Administrators, N.E.C.	390	2.3
Shipping and Receiving Clerks	60	0.4
Weighers	246	1.4
Foremen, N.E.C.	600	3.6
Machinists	30	0.2
Heavy Equipment Mechanics, Incl. Diesel	246	1.4
Checkers, Examiners, and Inspectors; Manufacturing	930	5.6
Cutting Operatives, N.E.C.	330	2.0
Mixing Operatives	2,520	15.2
Packers and Wrappers, Except Meat and Produce	66	0.4
Painters, Manufactured Articles	66	0.4
Machine Operatives, Miscellaneous Specified	8,460	50.9
Miscellaneous Operatives	1,446	8.7
Not Specified Operatives	270	1.6
Freight and Material Handlers	150	0.9
Vehicle Washers and Equipment Cleaners	60	0.4
Miscellaneous Laborers	60	0.4
Not Specified Laborers	60	0.2
	16,620	100%

APPENDIX D - TABLES

Table 1
Mean Body Weights (g) + SE of Rats Fed ETU in the Diet
(Graham et al, 1975)

Dietary level, ppm	No. of rats	2 months of diet	No. of rats	6 months of diet	No. of rats	12 months of diet
			Ma	les		
0 5 25 125 250 500	68 68 68 68 67 68	419 ± 5 421 ± 4 411 ± 4 421 ± 5 403 ± 4b 327 ± 4a	58 58 58	617 ± 10 613 ± 8 583 ± 8a 601 ± 9 579 ± 8b 509 ± 7a	45 48 47 46 44 47	
			r e	males		
0 5 25 125 250 500	68 68 68 68 68	270 ± 3 267 ± 3 259 ± 3b 254 ± 3a 245 ± 3a 231 ± 3a		371 ± 6 363 ± 7 357 ± 5 $342 \pm 5a$ $331 \pm 5a$ $326 \pm 5a$	47 48 46 48 46 46	466 ± 11 464 ± 11 442 ± 10 429 ± 11c 408 ± 9a 406 ± 8a

a Significantly different from control value, p = 0.001.

b Significantly different from control value, p = 0.01.

c Significantly different from control value, p = 0.05.

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Table 2
Mean Organ-to-Body Weight (g/kg) Ratios + SE of Charles River Rats Fed ETU for 2 Months, 6 months, and 12 months. (Ten Rats per Group) (Graham et al, 1975)

Dietary level, ppm		2 Months Thyroid(a)	6 Months Thyroid(a)	12 Months Thyroid(a)
	Males			
0		44.7 + 2.3	51.5 + 3.3	44.3 + 2.0
0 5		45.4 + 3.5	45.1 + 2.4	43.9 + 3.3
25		40.1 + 1.9	44.3 + 2.3	48.8 + 2.9
125		55.9 + 4.9	61.9 + 4.1	52.9 + 3.5b
250		$93.6 \pm 5.9d$	79.9 + 6.1c	87.7 + 13.2c
500		$102.9 \pm 8.3d$	$139.5 \pm 14.9b$	779.0 \pm 231.4b
	Females			
0	•	60.0 + 2.9	59.1 + 3.1	57.3 + 3.5
0 5		66.8 ± 3.5	65.9 + 4.4	56.4 + 3.3
25		66.2 + 3.3	59.8 + 3.8	56.8 + 3.3
125		78.4 + 3.3d	72.0 + 4.6d	68.6 + 4.1b
250		105.5 + 5.3d	93.5 + 4.1b	97.7 + 8.0e
500		171.3 + 15.51	174.6 + 21.5b	271.5 + 85.7b

a Thyroid ratios are expressed as mg/kg.

b Significantly different from control, p = 0.05.

c Significantly different from control, p = 0.01.

d Significantly different from control, p = 0.001.

Table 3
THYROID HORMONE LEVELS - AFTER 30 DAYS ON STUDY (Freudenthal et al, 1977)

		125-I	TBG	T-3	T-4	TSH
ETU		(percent	(percent T-3	(ng	(ug	(uIU
(ppm)	Sex	uptake)	bound)	percent)	percent)	per m1)
625	М	1.2 <u>+</u> 0.4*	60.3 + 2.6*	57.3 + 3.7*	0.9 + 0.6*	14.3 + 0.9*
625	F	2.1 + 1.4*	60.6 + 1.8	58.4 + 9.9*	1.1 + 1.0*	14.6 + 1.9*
125	M	3.6 ± 0.8	$60.7 \pm 1.3*$	71.1 ± 11.8	2.6 + 0.4*	23.3 ± 5.9
125	F	4.0 ± 1.7	$61.5 \pm 1.3*$	104.4 + 16.3*	$2.1 \pm 0.5*$	$18.3 \pm 4.0*$
25	M	2.9 ± 0.6	65.7 ± 2.3	67.1 + 15.9	5.6 ± 1.1	7.3 ± 1.5
25	F	3.2 ± 1.3	63.5 ± 2.0	86.3 ± 14.8	3.8 ± 0.8	5.1 ± 1.3
5	M	3.6 ± 0.6	69.3 ± 6.3	79.0 ± 8.1	4.7 ± 0.4	6.7 ± 1.4
5	F	3.8 + 1.0	68.9 ± 1.3	88.1 + 12.8	2.9 ± 0.9	4.9 ± 1.4
1	M	3.7 ± 0.7	64.5 ± 1.2	82.1 ± 13.0	5.1 ± 1.0	6.4 ± 0.8
1	\mathbf{F}	3.0 ± 0.5	63.4 ± 1.3	90.9 ± 11.3	3.5 ± 1.0	4.5 ± 0.9
0	M	3.6 ± 0.9	68.0 ± 5.6	76.0 + 11.8	5.0 ± 1.7	6.7 ± 2.5
0	F	3.5 ± 0.9	66.0 ± 5.2	83.2 ± 16.2	3.8 ± 1.4	6.0 ± 4.1
PTU (p	ropy1	thiourea)				
(ppm)						
125	M	2.9 ± 1.1	67.8 ± 2.0	$58.9 \pm 6.1*$	$0.9 \pm 0.2*$	
125	F	3.3 \pm 0.7	69.5 ± 1.6	$52.0 \pm 8.0*$	$0.7 \pm 0.1*$	

^{*}Significantly different (p = 0.05) from corresponding control. Student's t test was used to make comparison between the control and treated animals. All data reported as the mean, \pm S.D.

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Table 4
THYROID HORMONE LEVELS - AFTER 60 DAYS ON STUDY (Freudenthal et al, 1977)

		125 - I	TBG	T-3	T-4	THS
ETU		(percent	(percent T-3	(ng	(ug	(uIU
(ppm)	Sex	uptake)	bound)	Percent)	percent)	per ml)
625	М	1.9 + 1.0*	79.0 + 0.9	56.9 + 10.3*	0.2 + 0.1*	
625	F	2.4 + 1.8*	71.8 + 1.4	56.8 + 6.9*	0.2 + 0.1*	
125	M	3.6 + 1.4	66.3 + 1.3	79.8 + 28.1	2.8 + 0.5*	
125	F	3.3 + 1.0	66.3 + 2.1	78.5 + 28.6*	2.0 + 0.5*	-
25	M	3.2 + 0.7	76.9 + 1.6	86.4 + 7.6	2.8 + 0.5*	_
25	F	3.7 ± 1.3	74.7 + 1.7	126.2 + 15.1	2.6 + 0.5*	_
5	M	3.5 + 0.8	66.4 + 1.2	85.4 + 12.7	4.9 ± 0.5	_
5	F	4.0 + 0.8	64.0 + 1.8	118.5 + 14.3	2.9 + 0.9	_
1 1	M	2.7 + 0.6	70.4 + 1.2	80.3 + 12.0	4.9 + 0.7	_
1	\mathbf{F}	3.2 + 0.7	67.1 + 1.3	93.3 + 13.5	2.8 ± 0.8	_
0	M	4.3 ± 0.9	73.6 + 4.9	77.3 + 8.5	4.8 + 0.7	5.8 + 0.4*
0	F	3.5 ± 0.8	69.4 \pm 4.3	103.8 ± 19.1	3.3 ± 0.5	$6.4 \pm 0.9*$
PTU (ppm)						
125	M	3.9 + 1.6	61.7 + 2.6*	46.1 + 3.9*	1.2 + 0.2*	9.8 + 1.0*
125	F	5.4 + 1.7	62.2 + 2.1*	50.9 + 9.7*	0.8 + 6.1*	10.8 + 1.9*

^{*} Significantly different (p 0.05) from corresponding control.

^{**} TSH values to be used as control for PTU group.

Table 5
THYROID HORMONE LEVELS - AFTER 90 DAYS ON STUDY (Freudenthal et al, 1977)

(percent uptake) 2.5 ± 0. 3.7 ± 1. 2.8 ± 0. 3.9 ± 1. 3.3 ± 0. 3.4 ± 0. 3.7 ± 0.	8* 62.7 ± 68.9 ± 19 65.6 ± 28	-3 (ng percent) 2.0* 27.9 ± 13. 0.9* 35.2 ± 4. 1.1 86.1 ± 15. 1.6 105.5 ± 16. 1.5 79.4 ± 12. 2.3 108.7 ± 11. 0.8 76.1 ± 13.	$3*$ $1.1 \pm 0.6*$ 0 $2.3 \pm 0.6*$ 0 $1.6 \pm 0.3*$ 6 3.8 ± 1.0 6 2.9 ± 0.7	(uIU per ml) - - - - -
$ \begin{array}{c} 2.5 \pm 0. \\ 3.7 \pm 1. \\ 2.8 \pm 0. \\ 3.9 \pm 1. \\ 3.3 \pm 0. \\ 3.4 \pm 0. \end{array} $	8* 62.7 ± 68.9 ± 65.6 ± 65.6	2.0* 27.9 ± 13. 0.9* 35.2 ± 4. 1.1 86.1 ± 15. 1.6 105.5 ± 16. 1.5 79.4 ± 12. 2.3 108.7 ± 11.	3* 1.1 ± 0.6* 3* 1.1 ± 0.6* 0 2.3 ± 0.6* 0 1.6 ± 0.3* 6 3.8 ± 1.0 6 2.9 ± 0.7	per ml)
3.7 + 1. $2.8 + 0.$ $3.9 + 1.$ $3.3 + 0.$ $3.4 + 0.$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$3*$ $1.1 \pm 0.6*$ 0 $2.3 \pm 0.6*$ 0 $1.6 \pm 0.3*$ 6 3.8 ± 1.0 6 2.9 ± 0.7	- - - - -
3.7 + 1. $2.8 + 0.$ $3.9 + 1.$ $3.3 + 0.$ $3.4 + 0.$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$3*$ $1.1 \pm 0.6*$ 0 $2.3 \pm 0.6*$ 0 $1.6 \pm 0.3*$ 6 3.8 ± 1.0 6 2.9 ± 0.7	- - - -
$ \begin{array}{c} 2.8 + 0. \\ 3.9 + 1. \\ 3.3 + 0. \\ 3.4 + 0. \end{array} $	7 65.3 $\frac{1}{+}$ 1 64.3 $\frac{1}{+}$ 2 68.9 $\frac{1}{+}$ 1 65.6 $\frac{1}{+}$ 2	1.1 86.1 ± 15 . 1.6 105.5 ± 16 . 1.5 79.4 ± 12 . 2.3 108.7 ± 11 .	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	- - -
$3.9 \pm 1.$ $3.3 \pm 0.$ $3.4 \pm 0.$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1.5 $79.4 \pm 12.$ 2.3 $108.7 \pm 11.$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	- - -
$3.4 \pm 0.$	9 65.6 ± 2	2.3 108.7 \pm 11.	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	- -
	9 65.6 \pm 2		6 2.9 \pm 0.7	_
3.7 + 0.		0 76 1 1 12		
	· / * * · · ·	7.0 /U.I T IJ.	1 5.0 \pm 1.0	_
4.2 + 1.	1 70.1 ± 2	2.2 105.2 + 16.	6 3.0 + 0.7	_
3.5 + 0.	6 65.8 + 1	1.1 $68.7 + 9.$	9 4.0 + 1.0	_
		1.4 116.7 \pm 17.		-
3.8 + 0.	5 69.3 \pm 2	2.7 72.0 + 21.	5 4.5 + 0.8	$5.8 \pm 0.4*$
				$6.4 \pm 0.9*$
		1.3* 73.2 <u>+</u> 9.	$9 0.6 \pm 0.2*$	$9.4 \pm 1.3*$
$5.6 \pm 2.$	5 60.4 ± 1	1.7* 69.6 \pm 9.	$4* 0.4 \pm 0.2*$	$10.7 \pm 2.1*$
	3.5 + 0. $3.2 + 0.$ $3.8 + 0.$ $4.1 + 1.$ $4.7 + 1.$	$3.5 \pm 0.6 3.2 \pm 0.9 3.8 \pm 0.5 4.1 \pm 1.0 65.8 \pm 1.0 69.3 \pm 2.0 65.2 \pm $	$ 3.5 \pm 0.6 \\ 3.2 \pm 0.9 \\ 3.8 \pm 0.5 \\ 4.1 \pm 1.0 $ $ 65.8 \pm 1.1 \\ 68.7 \pm 9. \\ 63.1 \pm 1.4 \\ 116.7 \pm 17. \\ 69.3 \pm 2.7 \\ 65.2 \pm 2.9 \\ 106.8 \pm 25. $ $ 4.7 + 1.7 $ $ 59.1 + 1.3 * 73.2 + 9. $	3.5 + 0.6 3.2 + 0.9 3.8 + 0.5 4.1 + 1.0 65.8 + 1.1 68.7 + 9.9 63.1 + 1.4 116.7 + 17.6 2.5 + 0.7 72.0 + 21.5 4.5 + 0.8 4.1 + 1.0 65.2 + 2.9 106.8 + 25.0 3.3 + 0.8 4.7 + 1.7 59.1 + 1.3* 73.2 + 9.9 0.6 + 0.2*

^{*} Significantly different (p = 0.05) from corresponding control. **TSH values to be used as control for PTU group.

Table 6 Relative risk for development of tumors among mice treated with ETU when compared with negative controls (Innes et al, 1969)

Compound	Strain*	Strain* Mice with hep		ith hepa	omas Mice with pulmonary tumors		Mice with lymphomas			Total mice with tumors			
		M 	F	Sum	M	F	Sum	M 	F	Sum	M	F	Sum.
ETU	x	48.79*	Inf.+>	91.53+	1.31	5.45	3.03	0	1.59	1.06	14.82+	Inf.+>	27.44+
	Y	Inf.+>	68.82+	127.36+	1.16	0	1.05	13.47	6.28&	8.16+	Inf.+	27.96+	38.18+
	Sum	82.08+	158.90+	106.06+	1.22	3.49	1.87	4.52	3.83&	4.04&	24.04+	42.93+	32.75+

^{*}Strain X-(C57BL/6 x C3H/Anf) F1; strain Y-(C57BL/6 x AKR)F1. +Increased tumor yield significant at 0.01 level.

>Inf.- relative risk calculated as infinite. This figure may result from the absence of tumors in the control group and is not necessarily significant.

[&]amp;Increased tumor yield significant at 0.05 level.