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July 24, 1945

4346

1312

718387

Memorandum to: Dr. Dowdy

From: H. E. Stokinger

Re: Organ Weights of Laboratory Animals

The accompanying tables are in response to a request from Lt. Howland and include all the data we have available on the organ weights in their relation to body weights of laboratory animals. It is to be noted that all these animals have undergone exposures to T-dusts at approximately 20 mg/m^3, most of them for a period up to 30 days. Accordingly, the weights of the organs, expressed as percent of the body weight, will tend to be slightly greater than those of normal animals owing to the tendency for carcass weight, but not organ weight, losses to occur as a result of exposure.

Included also is a summarizing table of all this data expressing the mean percentage of the body weights of the organs.

Signed H.E.S.
H. E. Stokinger

HES/hmd

7-24-45
See accompanying letter
H.E.S.

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HES 7/26/45

Table I

MEAN PERCENTAGE OF BODY WEIGHT OF ORGANS OF VARIOUS ANIMAL SPECIES FOLLOWING EXPOSURE TO CERTAIN [redacted]-DUSTS

Organ	RAT Compound TF_4	TO_4	T_3O_8	TO_2F_2	N*	Average	GUINEA PIG Compound TF_4	TO_4	T_3O_8	TO_2F_2	N*	Average	RABBIT Compound TF_4	TO_4	T_3O_8	TO_2F_2	N*	Average
Lung	1.40	1.10	1.07	0.91	41	1.18	1.70	2.57	1.07	2.57	66	1.97	0.53	0.89	0.55	1.27	20	0.89
Kidney	1.16	1.03	0.95	1.07	42	1.08	1.06	1.07	0.97	1.70	65	1.18	0.74	0.94	0.69	0.87	20	0.82
Liver	4.83	5.40	5.36	5.58	35	5.15	4.84	5.35	2.94	5.00	56	4.83	3.75	4.45	5.18	3.86	17	4.25
Intestine				10.39	3	10.39										0.34	2	0.34
Stomach				0.55	5	0.55										0.81	3	0.81
Spleen				0.47	2	0.47										0.13	4	0.13
Brain				4.06	4	4.06										0.37	5	0.37
Tongue																0.14	2	0.14
Trachea																0.09	3	0.09
Thyroid																0.02	2	0.02
Heart																0.44	3	0.44
Pancreas				1.12	1	1.12										0.09	3	0.09
Adrenal				0.05	1	0.05										0.04	3	0.04
Eyes																0.27	2	0.27

Organ	CAT Compound TF_4	TO_4	T_3O_8	TO_2F_2	N*	Average	DOG Compound TF_4	TO_4	T_3O_8	TO_2F_2	N*	Average
Lung	1.59	1.03		0.98	9	1.21	2.29			1.38	3	1.68
Kidney	1.22	1.02		1.24	8	1.12	0.46			0.54	3	0.51
Liver	5.01	3.34		4.15	8	4.06	3.60			3.90	3	3.80
Heart	0.58			0.44	3	0.53	0.25			1.00	3	1.08
Adrenal	0.03			0.03	3	0.03	0.18			0.03	3	0.08
Spleen	0.25			0.18	3	0.23	0.16			0.19	3	0.18
Stomach	0.75			0.39	33	0.63	0.99				11	0.99
Eye	0.38			0.32	4	0.35				0.08	1	0.08
Tongue	0.22				2	0.22						
Brain	0.95			1.28	3	1.06	1.17			1.06	3	1.09
Pancreas	1.52			0.28	3	0.69	0.13			0.24	3	0.20
Thyroid	0.05			0.06	2	0.06	0.01			0.01	3	0.01
Testes	0.12				2	0.82						
Prostate										0.05	1	0.05
Trachea				0.09	2	0.09						
Gonad				0.25	2	0125						

* N = number of specim[redacted]

[redacted]

Table II

Weights of Organs and their Percentage of Body Weight of Animals Exposed to TF_4 for 30 Days

Body Weight	RATS Lung g	Lung % of Wt. Body Wt.	Kidney g	Kidney % of Wt. Body Wt.	Liver g	Liver % of Wt. Body Wt.
81	1.10	1.36	1.20	1.48	3.20	3.96
108	2.70	2.50	1.30	1.20	5.30	4.90
143	2.70	1.89	1.90	1.33	4.80	3.35
156	1.90	1.22	1.80	1.15	8.70	5.58
163	2.50	1.53	2.60	1.59	9.60	5.88
166	2.00	1.20	2.00	1.20	11.50	6.90
170			1.80	1.06		
175	2.50	1.43	1.90	1.09	9.90	5.66
180	2.00	1.11	1.90	1.05	10.80	6.00
180	2.50	1.39	2.50	1.39	8.40	4.65
192	2.10	1.09	1.50	0.78	8.90	4.63
196	2.20	1.12	2.00	1.02	1.80	0.92
218	2.80	1.28	1.90	0.87	7.40	3.39
218	2.30	1.05	2.00	0.92	9.80	4.50
219	2.20	1.00	1.80	0.82	11.60	5.30
227	2.80	1.23	2.90	1.28	13.60	6.00
232	2.30	1.00	2.40	1.06	12.20	5.26
255	4.40	1.73	4.30	1.69	12.30	4.80
257	5.50	2.14	2.50	0.97	13.90	5.40
Mean Percentage of Body Weight		1.40		1.16		4.83

Body Weight	GUINEA PIG Lung g	Lung % of Wt. Body Wt.	Kidney g	Kidney % of Wt. Body Wt.	Liver g	Liver % of Wt. Body Wt.
161	4.7	2.91	2.5	1.55	7.4	4.60
200	4.2	2.10	3.0	1.50	12.8	0.64
248	4.5	1.82	3.4	1.37	17.0	6.85
250	5.1	2.04	3.7	1.48	12.5	5.00
264	4.5	1.70	3.8	1.44	11.8	4.38
304	4.2	1.38	3.0	0.99	11.3	3.72
320	4.7	1.47	2.8	0.88	11.7	3.66
*325	5.5	1.69	3.6	1.10	20.6	6.34
336	8.9	2.65	3.5	1.04	19.2	5.70
338	5.8	1.72	2.8	0.83	19.2	5.68
339	5.9	1.74	3.6	1.06	14.3	4.20
340	4.7	1.38	2.5	0.73	13.5	3.96
363	6.3	1.73	3.8	1.05	22.3	6.15
365	4.6	1.26	2.1	0.57	22.9	6.27
374	4.9	1.31	3.1	0.83	14.2	3.80
376	5.9	1.57	3.3	0.88	17.6	4.70
400	4.7	1.18	3.0	0.75	18.5	4.63
403	5.3	1.31	4.7	1.16	22.0	5.45
436	6.2	1.42	4.2	0.96	18.0	4.10
*333	5.5	1.65	3.6	1.08	[illegible]	6.10
Mean Percentage of Body Weight		1.70		1.06		4.84

Body Weight	CATS Lung g	Lung % of Wt. Body Wt.	Kidney g	Kidney % of Wt. Body Wt.	Liver g	Liver % of Wt. Body Wt.
1500	12.3	0.82	10.1	0.67	76.3	5.08
1600	33.3	2.08	17.0	1.06	79.6	4.97
2964	55.5	1.87	57.3	1.93	147.2	4.97
Mean Percentage of Body Weight		1.59		1.22		5.01

Body Weight	RABBITS Lung g	Lung % of Wt. Body Wt.	Kidney g	Kidney % of Wt. Body Wt.	Liver g	Liver % of Wt. Body Wt.
1590	10.7	0.67	13.7	0.86	62.2	3.91
2900	12.8	0.44	19.7	0.68	104.4	3.60
3300	15.6	0.47	22.4	0.68		
Mean Percentage of Body Weight		0.53		0.74		3.75

Table II - continued

Organ	CATS (1600 g) Wt.	%	CATS (2964 g) Wt.	%	Mean for Cats	DOG (5400 g) Wt.	%
Heart	6.9	0.43	21.4	0.72	0.58	67.5	1.25
Adrenals			0.8	0.03	0.30	1.0	0.02
Spleen	2.1	0.13	11.3	0.37	0.25	8.9	0.16
Stomach	9.8	0.61	26.5	0.89	0.75	53.7	0.99
Eye	9.1	0.57	5.6	0.19	0.38		
Tongue	4.0	0.25	5.5	0.19	0.22		
Brain	18.0	1.12	22.8	0.77	0.95	63.0	1.17
Testes	1.7	0.10	4.1	0.14	0.12		
Pancreas	24.4	1.52			1.52	7.0	0.13
Thyroid	0.7	0.05			0.05	0.7	0.01
Lung						123.2	2.29
Kidney						25.0	0.46
Liver						194.1	3.60

Table III

Weights of Organs and their Percentage of Body Weight of Animals Exposed to TO_4 for 30 Days

Body Weight	Lung g	Lung % of Wt. Body Wt.	Kidney g	Kidney % of Wt. Body Wt.	Liver g	Liver % of Wt. Body Wt.
RATS						
146	1.8	1.23	1.7	1.16	7.8	5.35
166	1.4	0.84	1.7	1.02	9.6	5.78
168	1.7	1.01	1.7	1.01	8.5	5.05
178	2.3	1.29	2.0	1.12	10.1	5.68
205	2.3	1.12	1.7	0.83	10.4	5.15
Mean percentage of Body Weight		1.10		1.03		5.40
RABBITS						
1900	13.8	0.72	18.4	0.97	67.2	3.54
1950	19.4	0.99	18.4	0.94	102.0	5.22
2070	21.2	1.02	19.7	0.95	89.1	4.30
2200	25.3	1.15	21.7	0.99	101.8	4.62
2430	14.5	0.59	20.8	0.85	110.6	4.55
Mean percentage of Body Weight		0.89		0.94		4.45
CATS						
1560	19.6	1.26	16.2	1.04	60.7	3.90
2430	17.7	0.73	20.6	0.84	66.2	2.72
2720	15.8	0.58	18.0	0.66	97.0	3.56
4380	66.9	1.53	68.0	1.55	138.5	3.16
Mean percentage of Body Weight		1.03		1.02		3.34

Body Weight	Lung g	Lung % of Wt. Body Wt.	Kidney g	Kidney % of Wt. Body Wt.	Liver g	Liver % of Wt. Body Wt.
GUINEA PIGS						
105	9.76	9.3	3.5	3.34	21.17	20.05
252	5.50	2.18	3.3	1.31	11.20	4.45
262	5.91	2.26	2.1	0.80	15.67	5.97
288	11.10	3.86	2.7	0.93	14.80	5.13
288	6.80	2.36	2.0	0.69	15.00	5.20
320	5.20	1.63	1.8	0.56	13.20	4.12
350	8.90	2.54	3.4	0.97		
353	7.20	2.04	4.4	1.25	18.20	5.15
386	16.10	4.17	3.3	0.85	18.70	4.85
387	6.20	1.60			15.80	4.08
390	4.78	1.22	2.0	0.51	17.08	4.38
402	11.10	2.76	3.0	0.75	15.20	3.79
436	8.43	1.93	1.7	0.39	17.69	4.05
446	8.41	1.88	3.20	0.72	19.12	4.30
448	6.70	1.49	2.8	0.63	11.2	2.50
483	6.00	1.24	3.8	0.79	18.5	3.83
501	6.04	1.20	13.18	2.63	20.20	4.04
Mean percentage of Body Weight		2.57		1.07		5.35

Table IV

Weights of Organs and their Percentage of Body Weight of Animals Exposed to T_3O_g for 30 Days

Body Weight	RATS Lung g	Lung % of Wt. Body Wt.	Kidney g	Kidney % of Wt. Body Wt.	Liver g	Liver % of Wt. Body Wt.
130	3.0	2.30	1.3	1.00		
218	2.5	1.15	2.3	1.06		
232	2.4	1.03	3.0	1.29	14.2	6.12
238	1.4	0.59	1.6	0.67		
240	2.4	1.00	2.7	1.12	13.7	5.70
260	2.5	0.96	2.7	1.04	11.1	4.26
264	2.0	0.75	1.8	0.69		
270	1.9	0.70	2.2	0.81		
320	1.9	0.59	2.7	0.85		
Mean percentage of Body Weight		1.07		0.95		5.36
	RABBITS					
2048	9.8	0.49	13.6	0.67		
2150	14.5	0.68	14.4	0.67		
2440	9.8	0.40	18.9	0.78	89.8	3.68
2555	13.2	0.52	16.1	0.63	124.3	4.87
2695	18.3	0.68	19.5	0.73	188.3	7.00
Mean percentage of Body Weight		0.55		0.69		5.18

Body Weight	GUINEA PIGS Lung g	Lung % of Wt. Body Wt.	Kidney g	Kidney % of Wt. Body Wt.	Liver g	Liver % of Wt. Body Wt.
112	2.4	2.14	2.6	2.32		
216	2.6	1.20	2.8	1.30		
290	2.0	0.69	3.4	1.17	7.1	2.44
310	3.6	1.16	3.5	1.13	9.0	2.90
348	4.0	1.15	3.3	0.95		
376	4.1	1.09	4.0	1.06	11.8	3.14
388	4.4	1.13	3.0	0.77		
426	4.4	1.03	2.7	0.63		
472	3.9	0.83	3.5	0.74	12.9	2.73
486	5.3	1.09	3.5	0.72		
486	5.5	1.13	4.4	0.91	16.4	3.37
576	4.6	0.80	3.2	0.55		
620	3.9	0.63	4.9	0.79	18.6	3.0
658	6.7	1.02	5.2	0.79		
764	7.8	1.02	4.8	0.63		
Mean percentage of Body Weight		1.07		0.97		2.94

Table V

Weight of Organs and their Percentage of Body Weight of Animals Exposed to TO_2F_2 for 30 Days

Organ	RATS (155 g) Wt.	%	(169 g) Wt.	%	(178 g) Wt.	%	(181 g) Wt.	%	(186 g) Wt.	%
Lung	2.2	1.42	1.2	0.71	2.2	1.24	1.1	0.61	1.6	0.86
Kidney	2.5	1.61	1.4	0.83	1.8	1.01	2.1	1.16	2.3	1.24
Liver	10.3	6.50	9.8	5.80	9.2	5.05	10.0	5.52	10.9	5.85
Intestine	20.5	13.20	20.3	12.00	19.1	10.70	16.8	9.30	18.7	10.00
Stomach							1.0	0.55		
Brain							1.8	0.99		
Spleen					0.9	0.50	0.8	0.44		
Pancreas					2.0	1.12				
Adrenals					0.1	0.05				

Organ	RATS (193 g) Wt.	%	(226 g) Wt.	%	(231 g) Wt.	%	(279 g) Wt.	%	Means
Lung	1.9	0.98	2.1	0.93	1.9	0.82	1.8	0.65	0.91
Kidney	2.3	1.19	1.9	0.84	2.1	0.91	2.3	0.83	1.07
Liver	9.6	4.96	13.0	5.75	12.3	5.32	15.3	5.50	5.58
Intestine	17.0	8.80	20.7	9.20	23.8	10.30	27.8	10.00	10.39
Stomach	0.9	0.46	1.3	0.57	1.2	0.52	1.8	0.65	0.55
Brain	1.3	0.87	18.7	8.30			17.0	6.10	4.06
Spleen									0.47
Pancreas									1.12
Adrenals									0.05

Table V - continued

Organ	RABBITS (1840 g) Wt.	%	(1870 g) Wt.	%	(1890 g) Wt.	%	(2070 g) Wt.	%
Lung	19.0	1.03	21.5	1.15	34.0	1.80	15.2	0.73
Kidney	12.0	0.65	18.8	1.00	26.5	1.40	16.7	0.81
Liver	76.0	4.13	78.4	4.17	84.0	4.45	64.9	3.14
Intestine							3.7	0.18
Stomach			11.9	0.63			16.9	0.82
Spleen			0.7	0.04			0.7	0.03
Brain			6.9	0.57			7.2	0.35
Tongue							3.4	0.16
Trachea			2.9	0.15			2.8	0.13
Thyroid					0.4	0.02		
Heart			8.6	0.46			7.0	0.34
Pancreas			1.5	0.08			3.5	0.17
Adrenals			0.2	0.01			0.2	0.09
Eyes			5.8	0.31				

Organ	RABBITS (2210 g) Wt.	%	(2300 g) Wt.	%	(2320 g) Wt.	%	Mean
Lung	41.5	1.86	24.6	1.07	28.6	1.23	1.27
Kidney	16.5	0.75	17.5	0.76	16.0	0.69	0.87
Liver	76.6	3.46	90.0	3.92	87.8	3.78	3.86
Intestine	10.9	0.49					0.34
Stomach	21.8	0.99					0.81
Spleen	0.7	0.03			1.0	0.43	0.13
Brain	8.0	0.36	8.7	0.38	4.5	0.19	0.37
Tongue	2.7	0.12					0.14
Trachea	2.1	0.09					0.09
Thyroid					0.6	0.02	0.02
Heart	12.6	0.57					0.44
Pancreas	0.6	0.03					0.09
Adrenals	0.3	0.02					0.04
Eyes	5.0	0.22					0.27

[redacted]

Table V - continued

Organ	CATS (1985 g) Wt.	%	CATS (2325 g) Wt.	%	Mean
Lung	18.3	0.92	24.0	1.03	0.98
Kidney	24.7	1.24			1.24
Liver	82.1	4.15			4.15
Stomach	7.8	0.39			0.39
Spleen	3.7	0.18			0.18
Brain	25.6	1.28			1.28
Trachea	2.5	0.13	1.3	0.04	0.09
Thyroid	1.2	0.06			0.06
Heart	8.7	0.44			0.44
Pancreas	6.6	0.33	5.2	0.22	0.28
Adrenals	0.6	0.03	0.8	0.03	0.03
Eyes	4.3	0.21	9.8	0.42	0.32
Gonad	1.6	0.08	9.8	0.42	0.25

Organ	DOGS (5400 g*) Wt.	%	DOGS (7210 g**) Wt.	%	Mean
Lung	107.0	1.97	56.0	0.78	1.38
Kidney	30.3	0.56	37.0	0.51	0.54
Liver	215.0	4.00	270.0	3.80	3.90
Spleen	11.3	0.21	13.3	0.18	0.19
Brain	67.0	1.24	63.0	0.88	1.06
Thyroid	0.5	0.01	0.8	0.01	0.01
Heart	63.0	1.17	60.0	0.83	1.00
Pancreas	14.0	0.26	15.0	0.21	0.24
Adrenals	1.8	0.03	1.2	0.02	0.03
Eyes	4.1	0.08			0.08
Gonad					
Submaxillary Gland	5.5	0.10	7.8	0.18	0.14
Prostrate			3.6	0.05	0.05

* Original Weight - 6800 g.
** Original Weight - 8750 g.

[redacted]

Table V - Continued

Body Weight	GUINEA PIG Lung % of Wt. Body Wt.		Kidney % of Wt. Body Wt.		Liver % of Wt. Body Wt.	
130	2.0	1.54	2.0	1.54	5.7	4.40
130	2.8	2.08	2.4	1.85	7.8	6.00
132	4.4	3.34	2.5	1.88	7.4	5.60
138	5.0	3.62	2.5	1.81	7.6	5.50
140	6.5	4.65	2.2	1.57	6.8	4.85
144	5.8	4.03	2.5	1.74	7.2	5.00
160	5.9	3.70	2.8	1.75	8.0	5.00
164	4.3	2.62	2.9	1.77	6.6	4.02
165	3.8	2.30	2.8	1.70	6.5	3.94
180	4.1	2.28	3.9	2.16	15.2	8.41
184	2.9	1.58	3.1	1.69	11.5	6.25
190	3.7	1.95	3.1	1.63	7.2	3.78
204	2.1	1.03	2.8	1.37	8.0	3.92
214	4.8	2.24	2.9	1.35	8.3	3.38
Mean percentage of Body Weight		2.57		1.70		5.00

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PAGES

COPY NO. 4 OF 5 SERIES A

EIDMM-2a

MD.700.2

P. O. Box E

4 June 1945

JLF/mh

Subject: Maximum Allowable Concentration of Insoluble T Compounds in Factory Air.

To: The Area Engineer, Rochester Area, Rochester 7, New York (Attn: Lt. C. E. Coring)

1. This office is in receipt of a special report on maximum allowable concentration of certain T compounds in factory air, submitted by Dr. Carl Voegtlin and Dr. Harold Hodge on 21 February 1945. This report recommends that the maximum allowable concentration for chronic exposure to high-grade ore, T_3O_8, TO_2, and TF_4 be raised from 150 micrograms per cubic meter to 500 micrograms per cubic meter.

2. This recommendation is based on the results of exposure of animals to these substances, and careful observation of a large group of persons working in industry with these materials during the past two years.

3. Therefore, in the opinion of this office, the maximum allowable concentration for exposure to high-grade ore, T_3O_8, TO_2, and TF_4, should be increased to 500 micrograms per cubic meter. In view of the extreme difficulty in maintaining concentrations of 150 micrograms per cubic meter in industry, it is felt that such a change will be of definite benefit in expediting the war effort.

4. It is recommended that this change in the maximum allowable concentration be transmitted to the contractors under your supervision.

5. It is requested that this office be notified by indorsement of the action taken upon this recommendation.

For the District Engineer:

STAFFORD L. WARREN
Colonel, M.C.
Chief, Medical Section

SPECIAL REREVIEW
FINAL DETERMINATION
UNCLASSIFIED
2nd Review 10/2/80
By: [illegible] 10/2/80
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This document consists of 5 pages
No. 2 of 6 copies, Series A

P. O. Box 42, Station F
New York 18, New York
April 28, 1945

3642

File
7-27-45
CD Friedell

The District Engineer
U. S. Engineer Office
Manhattan District
P. O. Box E
Oak Ridge, Tennessee

Attention: Lt. Col. H. L. Friedell

Dear Colonel Friedell:

During a recent conversation, you indicated that you wished to have a statement of the steps by which we arrived at the opinion that 500 micrograms of T metal per cubic meter of factory air should be the maximum allowable concentration for T_3O_8, TO_2, TF_4 and high grade ore. We will attempt to present these steps in more or less orderly fashion.

1. The Definition of Acute T Poisoning. - We have now accumulated sufficient evidence to present a picture of acute T poisoning. Using soluble and toxic T compounds administered in a variety of ways the same pattern of toxic responses has inevitably emerged. The outstanding feature is the characteristic cycle of pathological changes in the kidney. These characteristic changes taken as a group provide us with a useful index by which we can measure the degree of toxicity of a given T compound.

2. Classification of T Compounds on the Basis of Toxicity. - Using a variety of techniques, we have studied a number of T compounds. For example, they have been fed to dogs and to rats; they have been applied to the skin and to the eyes of rabbits; they have been inhaled by dogs, cats, rabbits, guinea pigs, rats and mice. Using a number of criteria (mortality, weight loss, histopathological changes, chemical changes) we have repeatedly been able to arrange the T compounds in groups based on their relative abilities to produce acute T poisoning. These groups may be briefly indicated as follows:

Highly toxic:- TO_2F_2, T nitrate and TCl_4
Moderately toxic:- TO_3
Slightly toxic:- T_3O_8, TO_2, TF_4 and ore.

It should be emphasized that in certain tests, particularly the feeding and skin tests, the toxicity difference between the highly and slightly toxic groups is very large (10-100 to 1). Thus, from feeding studies we have gained the

[redacted]

To: Lt. Col. H. L. Friedell April 28, 1945

impression that T_3O_8, TO_2, and TF_4 are practically innocuous, whereas a few milligrams of TO_2F_2 ingested daily may be fatal.

3. Inhalation of High Dust Concentrations. - Rabbits, guinea pigs, rats and mice have been exposed to atmospheres containing about twenty mg./m^3 of T_3O_8, TO_2, TF_4 and ore. This concentration of dust represents a high level - 30 times the recommended maximum allowable concentration. Deaths occurred from each exposure so that at first glance this level may seem to be dangerous, however a closer examination of the data will serve to extenuate this conclusion.

Data on guinea pigs:

T_3O_8	-	1/12
TO_2	-	1/20
TF_4	-	0/18
Ore	-	2/20

Four of seventy guinea pigs exposed to the four compounds died.

Data on rats:

T_3O_8	-	0/12
TO_2	-	0/15
TF_4	-	2/17
Ore	-	1/20

Three of sixty-four rats exposed to the four compounds died.

Data on mice:

T_3O_8	-	0/12
TO_2	-	5/40
TF_4	-	0/20
Ore	-	2/40

Seven mice died of 112 mice exposed to the four compounds.

Grouping all of the guinea pigs, rats and mice together we find that 14 animals died of 248 exposed to the four compounds. This constitutes a mortality of about 6%. The interpretation of small mortality percentages is notoriously difficult. In fact, it is almost impossible to attach a meaningful degree of significance to the figure of 6% in this instance. It would require tests involving hundreds of animals of each species to be sure that the deaths recorded were due to T poisoning.

Data on rabbits:

T_3O_8	-	0/10
TO_2	-	6/10
TF_4	-	0/2
Ore	-	1/10

To: Lt. Col. H. L. Friedell 26 April 1945

One rabbit died of the 22 exposed to the three compounds T_3O_8, TF_4 and ore; this 5% mortality is subject to the same degree of uncertainty referred to above. TO_2 however, cannot be placed in the same category: six of ten rabbits exposed to TO_2 died. TO_2 appears to have a special lung toxicity for rabbits. The histopathological observations confirm this assumption; considerable lung damage was observed in these rabbits. The mortality data from the inhalation experiments pose a question as to the "practically innocuous" nature of these four compounds, however, these data can not be taken as clear cut evidence of a marked degree of toxicity upon inhalation.

4. Histopathological Findings. - Although the mortality observed in the several experiments may be considered to be of no great significance, the histopathological studies should not be slighted. Kidney injuries of variable degree of severity were observed in some animals as a result of exposure to each of the four compounds. The pathological picture was not clear cut, however, a summary may be presented as follows:

Kidney Pathology

Compound	Dogs	Rabbit	Cats	G.Pigs	Rats	Mice
T_3O_8	*	*	*	Mild & Infrequent	None	None
TO_2	*	Mild to moderately severe.	*	*	None	*
TF_4	None	Scattered mild	None	Scattered mild	Scattered mild	*
Ore	*	Moderate to moderately severe.	*	*	Inconstant mild to moderate.	*

* - No Data

These compounds failed to produce severe kidney injury regularly; nevertheless some injury was observed from each compound. It must be remembered that these injuries were produced by relatively high levels of T dust concentration. We do not have any information about exposures of the order of 0.5 mg/m^3. It is impossible to say that such a level would produce no injuries.

To: Lt. Col. H. L. Friedell 23 April 1945

5. Tentative Nature of Recommended Maximum Allowable Concentration. - Obviously more data are needed on the inhalation toxicity of these four compounds; especially are data needed on animals exposed to dust concentrations nearer that of the maximum allowable concentrations - 0.5 mg./m^3. We expect to conduct such studies within a year, but our attention has been directed so far to the compounds with higher priorities.

6. No Human Acute T Poisoning. - Heresay may have no place in a scientific discussion, but we have based our recommendations of a maximum allowable concentration in no small part upon the word of mouth reports that under the conditions of industrial practice no cases of human T poisoning have been discovered.

7. Is the Maximum Allowable Concentration Injurious? - From the close relationship which we have observed between exposure of animals to T compounds and injury especially to the kidney, we feel that it is entirely possible that slight injury may occur in industrial workers exposed to T dusts. We wish to point out the difference between "a safe level" and the "maximum allowable concentration". The safe level is a physiological entity, an exposure involving no injury. The maximum allowable concentration is an engineering bench mark. In industrial practice it may become necessary to strike a compromise between the air concentration which can be maintained during maximum production and the chance of injury to plant personnel.

The dust concentration may be so great during maximum production that it is prohibitively dangerous; the dust concentration of a safe level may be so low as to make volume production almost impossible. Under such circumstances it would be reasonable to set a maximum allowable concentration at such a level that production may proceed; if at this level the chance of injury is small.

8. Choice of Maximum Allowable Concentration. - It is our understanding that the maximum allowable concentration should be set as high as we can justify. We are aware that the setting of this maximum allowable concentration does not do away with the medical surveillance, use of respirators, personal hygiene and other health control measures. Consequently, evidence of any ill effects of a higher level will be promptly discovered and the permissable dust concentration reconsidered.

To: Lt. Col. E. L. Friedell 28 April 1943

9. War Measure. - One of the reasons why we have recommended 500 micrograms per cubic meter as the maximum allowable concentration is that we view this as an emergency war measure to expedite industrial production.

It would be hard to give an estimate as to how much weight we placed on each of these items. All taken together, they gave us a sufficient basis for our decision. We hope that this recapitulation has given you the information that you desired.

CARL VOEGTLIN,
Consultant.

HAROLD C. HODGE,
Chief Toxicologist.

DISTRIBUTION:
Copy 1 & 2 - Addressee
3 - Dr. Carl Voegtlin
4 - Dr. H. C. Hodge
5 - Dr. A. Dowdy
6 - A.E., Rochester Area

[redacted]

This document consists of 1 page
No 2 of 2 copies, Series A

WAR DEPARTMENT
UNITED STATES ENGINEER OFFICE
MANHATTAN DISTRICT
P. O. BOX 42
STATION F
NEW YORK, N. Y.

IN REPLY REFER TO: ENDH-3c
MD-700.2

16 April 1945

Subject: Toxicity of C-616, C-212 and C-215

MEMORANDUM to Files.

1. C-616:- All rabbits and mice died in one week's time when exposed to 3,000 micrograms per cubic meter. The experiments using 300 micrograms per cubic meter is contemplated and preliminary results will be ready in three weeks. Dr. Stokinger is convinced that although animals probably will not die, they will show definite toxicity with 150 parts per million.

2. C-212:- 1 p.p.m. killed all animals (rats and mice). 1/10 p.p.m. caused no deaths (rats, guinea pigs, mice and rabbits).

3. C-215:- 25 p.p.m. killed all animals in five to six days. 5 p.p.m. killed 10% of the animals but only head exposure was used in this experiment, and this technique could account for deaths. 3 p.p.m. caused no deaths but in Dr. Stokinger's opinion, could possibly be toxic.

B. J. MEARS,
Captain, Medical Corps.

Cc: Major J. L. Ferry

SPECIAL REREVIEW
FINAL DETERMINATION
UNCLASSIFIED
By: [signature] 10/10/80
Date: 10/2/80

[redacted]

The University of Rochester
School of Medicine and Dentistry
P. O. BOX 237, CRITTENDEN STATION
Rochester 7, N. Y.

August 9, 1944

Captain John L. Ferry
U. S. Engineer Office
P. O. Box E
Oak Ridge, Tennessee

Dear Captain Ferry:

The work of the dental research group has resulted in several interesting and important findings. Among these should be listed:

1. Industrial personnel exposed chronically to relatively large concentrations of HF in the air have an astonishing freedom from caries.

2. The teeth of our experimental animals, notably the continuously erupting incisors (for example, of the rat) show notably large deposits of T and may turn out to be one of our best indices of the relation of T to mineral metabolism. Thus, by studying the teeth we may find an exaggerated picture of what happens when T is deposited in bones.

I am sending along herewith quite a little volume of reports which have been submitted by Lt. Dale and, in some cases, by Dr. McCauley as a result of their various studies in reference to teeth. I wish to obtain from Colonel Warren authorization for whichever features of the study he thinks it well to continue. May I call your attention especially to the list of recommendations which include the following:

C. (1) A survey of the occurrence of lactobacilli. At the present time this seems to me academically interesting but not required.

C. (2) Urinalysis for fluorides. These arrangements have been made and this work will be done.

C. (3) Photographs of the lesions. Since this peculiar condition has not been previously described I believe that such photographs would be useful and serve as a basis for observing effects which may develop in the teeth of persons exposed to other fluorides, for example, PG.

C. (4) Analysis of the "gunk" on the teeth of fluoride workers. This would be in my opinion and that of Dr. Voegtlin's a useful study. It would involve scraping off some of the deposits, analyzing them for fluoride and in the case of PG workers for fluoride and T.

C. (5) Gross and Microscopic Studies of extracted teeth from PG workers. This should be carried far enough to find whether there are any evidences of abnormalities.

C. (6) The study of the effects of HF on teeth. This is a rather simple short-term experiment and might well yield interesting results.

I. (1) The analyses of our experimental animals for the T content of teeth and alveolar bone is being done. I think this work should be continued on a limited basis.

I. (2) Examination of workmen exposed to T should be a regular part of the health program wherever possible.

I. (3) Extracted teeth from T workers should be studied wherever possible.

I. (4) When these workers also are exposed to F it would be desirable to obtain F analyses on extracted teeth.

I enclose copies of eleven reports as follows:

A. "Preliminary Report of Oral Examinations of Twenty Government Employed Chemists". July 26-28, 1943.

B. "A Study of Oral Conditions in Laboratory Fluoride Workers" (at a University Site). August 30-31 and September 1-4, 1943. Preliminary Report.

C. "A Study of Dental Conditions in Workers Exposed to Dilute and Anhydrous Hydrofluoric Acid in Production". Preliminary Report. October 13-15, 1943.

D. "A Study of Dental Conditions in Workers Exposed to Dilute and Anhydrous Hydrofluoric Acid in Production". Radiographic Findings. December 31, 1943.

E. "A Study of Oral Conditions in Laboratory Fluoride Workers " (at a University Site). Findings from Oral Examinations. July 26-28, August 30-31 and September 1-4, 1943.

F. "A Study of Dental Conditions in Workers Exposed to Dilute and Anhydrous Hydrofluoric Acid in Production." January 6, 1944.

G. "A Study of Oral Conditions in Laboratory Fluoride Workers." Second Series of Examinations. January 24-25, February 28-29 and March 1-3, 1944.

H. "A Study of Dental Conditions in Workers Exposed to Dilute and Anhydrous Hydrofluoric Acid in Production. Statistical Report. 1 April 1944.

I. "Proposed determinations of T in extracted teeth and alveolar bone of T-employees as a possible index of bodily storage". June 29, 1944.

J. "Preliminary Dental Report on the Distribution of T and F in the Teeth of Animals Exposed to T-compounds." June 27, 1944.

K. "Dental Histology Report of Animals Subjected to TF_4 and C-212 by Inhalation". May 25, 1944.

Yours very truly,

Harold C. Hodge
Chief Pharmacologist