

**APPLIED
EPIDEMIOLOGY
INC.**



February 27, 1998

Ms. Wendy K. Sherman
Manager, Vinyl Chloride Health Committee
Chemical Manufacturers Association
1300 Wilson Blvd.
Arlington, VA 22209

Dear Ms. Sherman:

Enclosed please find our "baseline" results for the CMA Vinyl Chloride Study cohort. Specifically, these results reflect our re-calculation of all causes of death reported by Dr. Wong through 1982, as well as several additional causes of death not previously analyzed or reported (due to limitations of the available analytical packages of the time) and with at least two observed or two expected deaths. Our cohort differs from that analyzed by Dr. Wong in that we have identified and corrected numerous errors, restored several hundred cohort members not included in Dr. Wong's analyses and discovered some additional deaths. The details of these differences have been presented in earlier progress reports, and the final description will be detailed in our final report to CMA.

Three columns of results are presented in the accompanying table: the first column contains results based on our cleaned and expanded cohort using the United States mortality rates as the reference (methodologically most comparable to Dr. Wong's results); the second set contains results using rates for the states in which each plant was/is located; and the third reflects Dr. Wong's results.

Almost universally, our results mirror those of Dr. Wong. Most exceptions are due to some re-arrangement of specific causes of death within broader disease categories, often reflecting the way deaths are coded over different time periods and in different states (e.g., liver cancers and cardiovascular disease deaths).

The one result which might be considered a "new" finding is the elevated SMR for "connective and soft tissue" cancers (three-fourths of the way down on page two), with SMR=381 using the United States reference rates (95% confidence interval 153 to 785) and SMR=367 using state referent rates (95% confidence interval 147 to 755), based on seven observed deaths due to these cancers.

(continued)

P.O. BOX 2424 AMHERST, MA 01004



(413) 256-3556 • FAX (413) 256-3503

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(Ms. Sherman, page 2)

Biologically, this observed excess might be related to the well-known association between vinyl chloride exposure and angiosarcoma of the liver, as angiosarcomas (tumors of the blood vessels) occurring outside of the liver are classified as soft tissue sarcomas. On the other hand, deaths due to angiosarcoma of the liver but erroneously recorded on a death certificate simply as "angiosarcoma" without specifying "of the liver" will be classified as a soft tissue sarcoma as well. Unfortunately, it is not possible to determine from the death certificate whether this has occurred.

Nevertheless, this association has not been reported elsewhere to date; therefore, we believe that you may have some obligation to report this finding to EPA under the Toxic Substances Control Act.

Please feel free to call if you have any questions about these baseline results. Thank you.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Kenneth A. Mundt". The signature is fluid and cursive, with the first name "Kenneth" and last name "Mundt" clearly distinguishable.

Kenneth A. Mundt, Ph.D.

enclosure

Applied Epidemiology, Inc. baseline study results and Wong et al., 1992 results: Observed (Obs) and expected (Exp) deaths, standardized mortality ratios (SMR's) and ninety-five percent confidence intervals (95% CI's) using U.S. white male mortality rates, plant state-specific white male mortality rates, for follow-up through December 31, 1982

Cause of death	Applied Epidemiology, Inc. baseline analysis							Wong et al., 1992			
	U.S. reference rates				State reference rates			U.S. reference rates			
	Obs	Exp	SMR	95% CI	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
All causes	1569	1734.92	90	86-95	1876.87	84	80-88	1536	1705.27	90	86-95
All malignant neoplasms	389	363.09	107	97-118	380.46	102	92-113	359	341.73	105	94-117
Cancer of:											
Buccal cavity & pharynx	13	11.81	110	59-188	11.61	112	60-192	12	11.55	104	54-181
Tongue	4	2.74	146	40-374	2.56	156	43-400	4	nr	--	
Other parts buccal cavity	3	3.15	95	20-278	2.98	101	21-294	3	nr	--	
Pharynx	5	5.66	88	29-206	5.79	86	28-202	4	nr	--	
Digestive organs & peritoneum	106	94.82	112	92-135	91.43	116	95-140	99	89.21	111	90-135
Esophagus	7	8.59	81	33-168	8.37	84	34-172	7	8.07	87	35-179
Stomach	11	16.10	68	34-122	14.78	74	37-133	10	16.01	63	30-115
Intestine, except rectum	21	31.44	67	41-102	29.57	71	44-109	20	28.79	70	42-107
Rectum	5	9.71	51	17-120	8.89	56	18-131	5	9.91	50	16-118
Liver & biliary tract	39	8.11	481	342-657	9.11	428	304-585	37	5.77	641	450-884
Pancreas	18	19.21	94	55-148	18.89	95	56-151	16	18.40	87	50-141

Cause of death	Applied Epidemiology, Inc. baseline analysis							Wong et al., 1992			
	U.S. reference rates				State reference rates			U.S. reference rates			
	Obs	Exp	SMR	95% CI	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
Peritoneum & other digestive organs	5	1.65	302	98-706	1.82	274	89-640	4	nr	--	
Respiratory system	128	132.71	96	80-115	151.35	85	71-101	115	122.25	94	78-113
Larynx	3	5.44	55	11-161	5.94	50	10-148	3	5.24	57	12-168
Trachea, bronchus & lung	122	125.56	97	81-116	143.58	85	71-101	111	115.87	96	79-116
Other respiratory system	3	1.71	176	36-513	1.83	164	34-480	1	nr	--	
Prostate	15	16.55	91	51-149	15.59	96	54-159	15	15.20	99	55-163
Kidney	11	9.53	115	58-207	9.73	113	56-202	11	9.06	121	61-217
Bladder	6	8.58	70	26-152	8.34	72	26-157	5	8.46	59	19-138
Skin	7	8.28	85	34-174	8.34	83	33-171	6	7.36	82	30-178
Eye	2	0.32	628	76-2269	0.42	475	58-1717	0	0.31	0	
Brain & other nervous system	22	13.61	162	101-245	13.05	169	106-255	23	12.76	180	114-271
Thyroid	2	0.74	269	33-972	0.73	274	33-989	2	0.68	293	36-1059
Bone	2	1.66	120	15-434	2.19	91	11-330	2	1.81	111	13-399
Connective & soft tissue	7	1.84	381	153-785	1.91	367	147-755	6	nr	--	
Lymphatic & hematopoietic	37	36.91	100	71-138	37.29	99	70-137	37	36.28	102	72-141
Lymphosarcoma/reticulosarcoma	10	7.77	129	62-237	7.72	130	62-238	11	7.98	138	69-247
Hodgkin's disease	3	5.16	58	12-170	5.31	57	12-165	3	5.45	55	11-161
Leukemia & aleukemia	12	14.73	81	42-142	15.03	80	41-139	13	13.94	93	50-159

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	U.S. reference rates				State reference rates			U.S. reference rates			
	Obs	Exp	SMR	95% CI	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
Other lymphatic & hematopoietic	12	9.25	130	67-227	9.23	130	67-227	10	8.37	119	57-220
Unspecified	29	22.37	130	87-186	25.13	115	77-166	23	nr	--	
Benign & unspecified nature neoplasms	7	5.70	123	49-253	5.54	126	51-260	4	5.08	79	21-201
Unspecified nature of eye, brain & other nervous system	4	2.68	149	41-382	2.80	143	39-365	1	nr	--	
Other	3	2.07	145	30-424	2.01	149	31-436	3	nr	--	
Diabetes mellitus	23	23.89	96	61-144	25.38	91	57-136	22	23.52	94	59-142
Diseases of the blood & blood forming organs	2	4.17	48	6-173	4.37	46	6-165	2	3.76	53	6-192
Mental, psychoneurotic & personality disorders	7	12.74	55	22-113	13.15	53	21-110	4	11.80	34	9-87
Alcoholism	4	8.86	45	12-116	9.20	43	12-111	3	nr	--	
Other mental disorders	3	3.87	77	16-226	3.94	76	16-222	1	nr	--	

Cause of death	Applied Epidemiology, Inc. baseline analysis							Wong et al., 1992			
	Obs	U.S. reference rates			State reference rates			U.S. reference rates			
		Exp	SMR	95% CI	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
Diseases of the nervous system & sense organs	14	17.29	81	44-136	17.40	80	44-135	15	nr	--	
Multiple sclerosis	3	2.31	130	27-380	1.87	161	33-470	3	nr	--	
Other diseases of nervous system & sense organs	11	14.98	73	37-131	15.53	71	35-127	12	nr	--	
Diseases of the heart	642	680.17	94	87-102	735.95	87	81-94	601	nr	--	
Rheumatic heart disease	12	18.71	64	33-112	16.46	73	38-127	14	19.33	72	40-122
Ischemic heart disease	535	583.71	92	84-100	630.80	85	78-92	488	597.73	82	75-89
Chronic disease of endocardium	5	3.55	141	46-329	3.17	158	51-368	3	nr	--	
Other myocardial degeneration	3	7.89	38	8-111	5.84	51	11-150	31	nr	--	
Hypertension with heart disease	23	15.20	151	96-227	14.50	159	101-238	23	nr	--	
Other heart diseases	64	51.12	125	96-160	65.17	98	76-125	42	nr	--	
Other diseases of the circulatory system	109	129.73	84	69-101	143.51	76	62-92	103	nr	--	
Hypertension without heart disease	3	4.53	66	14-193	5.06	59	12-173	8	nr	--	
Cerebrovascular disease	78	86.64	90	71-112	96.46	81	64-101	70	91.93	76	60-96
Diseases of arteries, veins & pulmonary circulation	28	38.55	73	48-105	41.99	67	44-96	25	nr	--	

Cause of death	Applied Epidemiology, Inc. baseline analysis							Wong et al., 1992			
	U.S. reference rates				State reference rates			U.S. reference rates			
	Obs	Exp	SMR	95% CI	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
Diseases of the respiratory system	70	91.93	76	59-96	111.60	63	49-79	70	87.61	80	62-101
Pneumonia	16	31.54	51	29-82	34.41	47	27-76	15	31.94	47	26-78
Chronic & unspecified bronchitis	2	4.38	46	6-165	5.44	37	4-133	2	nr	--	
Emphysema*	17	20.12	84	49-135	23.45	72	42-116	17	nr	--	
Asthma	1	3.00	33	1-185	3.76	27	1-148	1	2.89	35	1-192
Pneumoconioses & other respiratory diseases (includes COPD)	33	30.30	109	75-153	41.21	80	55-112	35	nr	--	
<i>Emphysema & COPD*</i>								41	22.83	180	129-244
Diseases of the digestive system	63	97.55	65	50-83	93.36	67	52-86	60	95.58	63	48-81
Diseases of stomach & duodenum	9	12.11	74	34-141	12.02	75	34-142	8	11.15	72	31-114
Hernia & intestinal obstruction	2	3.81	53	6-190	3.83	52	6-189	2	nr	--	
Cirrhosis of the liver	38	56.70	67	47-92	50.91	75	53-102	35	56.06	62	43-87
Other digestive system diseases	14	24.93	56	31-94	26.60	53	29-88	14	nr	--	
Diseases of the genitourinary system	8	19.80	40	17-80	21.55	37	16-73	9	20.41	44	20-84
Chronic/unspecified nephritis	4	9.41	43	12-109	10.11	40	11-101	4	8.29	48	13-123
Other genitourinary diseases	3	3.77	79	16-232	4.33	69	14-203		nr	--	

Cause of death	Applied Epidemiology, Inc. baseline analysis							Wong et al., 1992			
	U.S. reference rates				State reference rates			U.S. reference rates			
	Obs	Exp	SMR	95% CI	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
Diseases of musculoskeletal system & connective tissue	1	3.15	32	1-177	3.28	30	1-170			--	
Symptoms & ill-defined conditions	7	21.51	33	13-67	26.68	26	11-54	10	21.79	46	22-84
All external causes	183	226.58	81	69-93	256.67	71	61-82	168	225.97	74	64-87
Accidents	117	153.26	76	63-91	175.92	67	55-80	108	150.16	72	59-87
Violence	66	73.32	90	70-114	81.75	81	62-103	60	nr	--	
Suicide	49	53.89	91	67-120	55.51	88	65-117	46	52.78	87	64-116
Homicide	17	19.43	87	51-140	26.24	65	38-104	14	nr	--	
Other causes	15	25.00	60	34-99	25.49	59	33-97	7	nr	--	
Unknown	28							97			

nr=no rates available for category of death

* In the NIOSH categories of death (used in AEI baseline analysis), deaths from emphysema (ICD-7 527.1; ICD8 492; ICD9 492) are included in *Emphysema* and deaths from COPD (ICD-7 527.2; ICD-8 519.2; ICD-9 496) are included in *Pneumoconioses & other respiratory diseases*. In the Monson categories of death (used in Wong et al. analysis), *Emphysema & COPD* includes deaths from any of the following: Pulmonary collapse (ICD-7 527.0); Emphysema without mention of bronchitis (ICD-7 527.1); Other diseases of the lung (includes COPD) (ICD-7 527.2).

VINYL CHLORIDE HEALTH COMMITTEE ACTIVITIES

07/28/97

timeline for finalizing the Guidelines. IMPORTANCE	DEADLINES
EPA / PETITION TO RAISE THE "REPORTABLE QUANTITY" (RQ) OF VINYL CHLORIDE The Vinyl Institute will take the lead on determining whether a petition to raise the RQ is feasible. The VCHC will provide technical expertise if the VI decides that it is feasible. Caffey Norman will provide background on the criteria for determining the RQ. IMPORTANCE	ACTION ITEMS DEADLINES
EPA / AIR TOXICS PROGRAM EPA identified vinyl chloride and 36 other chemicals as "high priorities" for regulation under its Air Toxics Program. The Agency plans to develop a comprehensive integrated strategy for establishing an "air toxics management model." Caffey Norman provided background on EPA's activities with the Air Toxics Program, and CMA has asked to be a stakeholder. IMPORTANCE	ACTION ITEMS DEADLINES
ASSOCIATION OF PLASTICS MANUFACTURERS IN EUROPE (APME) / REGISTRY OF CASES OF ANGIOSARCOMA APME has developed a protocol for the maintenance of a register of cases of angiosarcoma related to PVC production. IMPORTANCE	ACTION ITEMS CMA will monitor the development of the registry. DEADLINES
AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS (ACGIH) / INITIATIVE TO LOWER THE THRESHOLD LIMIT VALUE (TLV) FOR VINYL CHLORIDE The concern from ACGIH is based on an article by Simonato, et al. in the Scand J. Work & E H ACGIH met on October 5, 6, 7, 1996 in Philadelphia. Peter de la Cruz of Keller & Heckman (Vinyl Institute) responded to Dr. William Waddell of the Univ. of Louisville (ACGIH) for Frank Borell	ACTION ITEMS The Committee will examine the Simonato paper and make contact with William Waddell to propose presenting information to ACGIH. DEADLINES

VINYL CHLORIDE HEALTH COMMITTEE ACTIVITIES

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IMPORTANCE	
CALEPA / DEVELOPMENTAL AND REPRODUCTIVE TOXICANT (DART) IDENTIFICATION COMMITTEE PRIORITY LIST Vinyl chloride is a potential candidate for listing under Proposition 65. The VCHC submitted comments to CalEPA. IMPORTANCE	ACTION ITEMS The Committee will monitor this issue. DEADLINES