

MEMORANDUM

PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

TO : Deputy Director, NIOSH

DATE: August 24, 1976

THROUGH: Chief, Industry-wide Studies Branch, DSHEFS, NIOSH *gfw*

THROUGH: Chief, Biometry Section, IWSB, DSHEFS, NIOSH *gfw*

THROUGH: Director, Division of Surveillance, Hazard Evaluations and Field Studies, NIOSH

FROM : Epidemiologist, Biometry Section, IWSB, DSHEFS, NIOSH *PJB*

SUBJECT: Review of DCMA Lead Chromate Report

The "Epidemiological study of Lead Chromate Plants" prepared by Equitable Environmental Health, Inc. examines the mortality experience of 577 lead chromate workers. The study population is defined as any male worker who had been exposed to lead chromate for at least six months prior to December, 1974. Ninety-five percent of 548 workers' vital status was ascertained and 50 deaths (with certificates) had occurred in this group. The study population was of necessity divided into three groups since the workers were employed in three separate plants as follows:

	<u>Total</u>	<u>Hired before 1960</u>	<u>Deaths/Certificates</u>
Plant 1	238 workers	131	12 deaths
Plant 2	152 workers	45	5 deaths
Plant 3	158 workers	158	33 deaths
	<u>548 workers</u>	<u>334</u>	<u>50 deaths</u>

The analytical section of this study, despite the small numbers of deaths involved, show excesses of both respiratory and digestive (primary stomach) cancer. Plants 1 and 2 had exposures solely to lead chromate. Plant 3 had mixed exposures to lead chromate and to zinc chromate, (refer to attached table) with only one worker having sole exposure to lead chromate. (He died of lung cancer).

The most apparent serious deficiency of this study is the short latent period of this worker cohort. Table 5 of the study shows it to be 17 years at most. A further complication is that most of the workers with the longest latency periods fall into the mixed exposure group at plant 3. The relatively purer exposure of workers at plants 1 and 2 is diluted by recent hires, and short term employees resulting in a cohort of only 176 workers (total from both plants combined) who were hired prior to 1960. Plant 3's total is 158 workers hired before 1960. Of the workers who were hired before 1960 and worked 10 years or more - plants 1 and 2 total 59, whereas plant 3 has 138. (Refer to attached table).

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It is a generally accepted theory that the latency period (time from first exposure to the onset of disease or death) for occupationally induced cancer is usually in the range of 20-35 years. These lead chromate workers have most likely not had sufficient latency for any significant excesses to appear. 2

Other noticeable limitations to this data set are the extremely small sample sizes, as stated above. Essentially there are three cohorts which must be analyzed individually - refer to above for numbers of workers by plant. The possibility of Type II Error, or failing to detect a significant difference when one does in fact exist, should be considered in the evaluation of this data set, due to the very small numbers of deaths involved. 3

No age distribution for this cohort is presented anywhere in the study. Racial differences are presented as follows: Plant 1 - "overwhelmingly white", Plant 2 - "conservative estimate is that half of the plant population is non-white", Plant 3 - "is 50% non-white". Nevertheless, the authors chose to use the crude death rates (for the state in which each plant was located) to generate expected deaths. The reliability of the SMR's generated using this type of control population, which is unadjusted for confounding variables such as age and race is questionable. The contributory role associated with both age and race, in both respiratory and digestive tract cancer is well documented. 4

When the authors used age-sex-race-adjusted rates for the S.M.S.A. for each plant location as a control; the SMR's changed considerably, a drastic illustration of the effect of the choice of an appropriate control population on statistical analysis. Considerable bias may well be present in the control group. 5

Another limitation on respiratory cancer inferences is the confirmed smoking history of nearly all those who died of lung cancer. This problem could probably be resolved if latency were longer and if cell types of lung cancers were given.

In spite of the above methodological problems, an increasing gradient of the SMR's was observed with increasing time from first exposure to lead chromate at plants 1 and 2. The mixed exposure to zinc chromate and lead chromate at plant 3 resulted in consistently elevated SMR's for respiratory and digestive cancer - consistently elevated due to cohort composition, a statistical artifact. If the records available at plant 3 (prior to 1957, plant began in 1941) had been included in this study, more of a gradient in cancer deaths would probably have shown up in the analysis, similar to that observed in plants 1 and 2. 6

The results of using S.M.S.A.'s for a control population and thereby controlling for variables such as age, race, sex are interesting. The SMR calculated for respiratory cancer dropped somewhat, but still shows an excess. For plant 3, the SMR for digestive cancer elevated to an 8-fold excess (from 209.9 to 778.5). 7

The authors state that since no mention of stomach cancer as a consequence of chromate exposure is made in the scientific literature on zinc chromate and since no stomach cancer was found in plant 1 and 2, it is unlikely that these stomach cancer deaths are attributable to either of these two exposures. One purpose of epidemiologic research in the field of occupational health is to uncover associations between certain chemicals or compounds and the resultant health status of workers occupationally exposed to these substances. Therefore, it does not seem justifiable to rule out any association between stomach cancer and the exposures to zinc chromate in plant 3 just because there has been no previous mention in the scientific literature. An 8-fold excess of stomach cancer deaths in any plant can not be lightly passed over. A more thorough detailed investigation of work history and other factors should be done, as the authors mention.

The authors contend that no definitive conclusions can be made from this study, due to the small numbers involved. But, the respiratory cancer excess holds up for both the 12 deaths in plant 1 and the 33 deaths in plant 3, showing a gradient with increased exposure and latency, which should be investigated further. A re-analysis of this data is in order.

This reviewer contends that the latency was not long enough, sample size was too small and that the control population was not well enough defined for a clear conclusion to be made concerning the exact magnitude of cancer risk being experienced by workers exposed to lead chromate or zinc-lead-chromate. A more rigorous data presentation and re-analysis of mortality data should probably be done in order to clarify the excesses of respiratory and digestive cancer already demonstrated by way of this insensitive study.

Cynthia Robinson
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SUMMARY OF STUDY RESULTS

PLANT 1

PLANT 2

PLANT 3

	Lead Chromate				Lead Chromate				Lead and Zinc Chromate						
	Digestive Cancer Obs/Exp	SNR	No. of Workers	Respiratory Cancer Obs/Exp	SNR	Digestive Cancer Obs/Exp	SNR	No. of Workers	Respiratory Cancer Obs/Exp	SNR	Digestive Cancer Obs/Exp	SNR	No. of Workers	Respiratory Cancer Obs/Exp	SNR
PbCr workers - using crude state rates for 1969	0/1.0	0.0	238	2/1.1	213.9	0/0.4	0.0	152	2/0.4	566.0	6/2.9	203.7	158	6/2.5	237.1
PbCr workers - hired before 1960 using crude state rates	0/0.9	0.0	131	2/1.1	216.2	0/0.3	0.0	45	0/0.3	0.0	6/2.9	203.7	158	6/2.5	237.1
PbCr workers - hired before 1960, employed ≥ 10 years using crude state rates	0/0.6	0.0	37	2/0.7	329.7	0/0.3	0.0	22	0/0.3	0.0	6/2.9	209.9	138	6/2.4	244.1
PbCr workers - hired before 1960 - employed ≥ 10 years using SWSA, assuming 50% non- whites, for year 1970, age-adjusted.			37	2/1.1	200.6	0/0.6	0.0	22			5/0.6	778.3	138	6/3.2	189.1

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CT: Review of DCMA Lead Chromate Report

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The analytical section of this study, despite the small numbers of deaths involved, show excesses of both respiratory and digestive (primary stomach) cancer. Plants 1 and 2 had exposures solely to lead chromate. Plant 3 had mixed exposures to lead chromate and to zinc chromate, (refer to attached table) with only one worker having sole exposure to lead chromate. (He died of lung cancer).

The most apparent serious deficiency of this study is the short latent period of this worker cohort. Table 5 of the study shows it to be 17 years at most. A further complication is that most of the workers with the longest latency periods fall into the mixed exposure group at plant 3. The relatively purer exposure of workers at plants 1 and 2 is diluted by recent hires, and short term employees resulting in a cohort of only 176 workers (total from both plants combined) who were hired prior to 1960. Plant 3's total is 158 workers hired before 1960. Of the workers who were hired before 1960 and worked 10 years or more - plants 1 and 2 total 59, whereas plant 3 has 133. (Refer to attached table).

*Two workers
one died of lung cancer*

*There is nothing that could
be construed as indicating
that the latent period
was 17 years at most.*

226 workers

It is a generally accepted theory that the latency period (time from first exposure to the onset of disease or death) for occupationally induced cancer is usually in the range of 20-35 years. These lead chromate workers have most likely not had sufficient latency for any significant excesses to appear.

Other noticeable limitations to this data set are the extremely small sample sizes, as stated above. Essentially there are three cohorts which must be analyzed individually - refer to above for numbers of workers by plant. The possibility of Type II Error, or failing to detect a significant difference when one does in fact exist, should be considered in the evaluation of this data set, due to the very small numbers of deaths involved.

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The results of using S.M.S.A.'s for a control population and thereby controlling for variables such as age, race, sex are interesting. The SMR calculated for respiratory cancer dropped somewhat, but still shows an excess. For plant 3, the SMR for digestive cancer elevated to an 8-fold excess (from 200.9 to 778.3).

The SMR 209.9 is for all digestive cancer; whereas 778.3 is an SMR for stomach cancer only.

Some occupational cancers have latent periods shorter than 20 years; e.g. in Health of Workers in Chromate Producing Industry, USPHS, No. 192 (1953) workers in 15-34 yr age group had the greatest excess of cancer deaths of all age groups. 15-25 yr has been suggested as a more common range.

Age was taken into account. See "Study design", p.2.

The description of the change as "considerable" is questioned.

Not an artifact. Rather, a true picture for plant 3 explainable by the longer average latent period here.

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	Digestive Cancer			Respiratory Cancer			Digestive Cancer			Respiratory Cancer		
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PbCr workers - using crude state rates for 1960	0/1.0	0.0	238	2/1.1	213.9		0/0.4	0.0	152	2/0.4	566.0	6/2.9
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PbCr workers - hired before 1960 - employed ≥ 10 years using SMMA, assuming 50% non-whites, for year 1970, age-adjusted.			37	2/1.1	200.6		0/0.6	0.0	22			5/0.6

These figures relate to respiratory cancer, not digestive cancer.

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not