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PREFACE

Increasing international concern is being expressed regarding the contamination of the environment with polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans because certain of these chemicals have been shown to be highly toxic to animals and are ubiquitous in the environment. They are known to be distributed as contaminants of commercial products and as by-products from combustion processes.

A considerable volume of information has accumulated on these chemicals in the past two decades, particularly for the most toxic of them, 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD). However, this body of knowledge has not succeeded in resolving genuine judgmental differences among experts in the field as to the degree of hazard to human health and the environment. In light of the widespread public concern, it is clearly imperative to come to grips with the continuing scientific controversy, to review the data, assess the issues, to see where areas of agreement exist, and where further research is needed to resolve remaining areas of disagreement.

This volume represents an effort to contribute to these goals. The volume contains the Proceedings from an International Symposium on Chlorinated Dioxins and Related Compounds which was held October 25 to 29, 1981, in Arlington, Virginia. The objectives of the meeting were to bring together scientists from a wide range of disciplines, all of whom were directly concerned with one aspect or another of the dioxin problem, to review the existing information, evaluate controversial data, present new data, identify areas of agreement, and indicate directions for future research. The 56 papers and panel reports that comprise this volume testify to the success of the Symposium.

The meeting was divided into nine sections:

- Definition of the Problem
- Analytical Chemistry
- Environmental Chemistry
- Animal Toxicology

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A MORTALITY STUDY OF WORKERS EMPLOYED AT THE
MONSANTO COMPANY PLANT IN NITRO, WEST VIRGINIA

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BACKGROUND

The compound 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is a highly toxic impurity that is formed in trace quantities during the production of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). Exposure to TCDD can cause chloracne, a skin disorder characterized by comedones, cysts, and abscesses.¹ Outbreaks of chloracne have been reported among workers associated with the production of 2,4,5-T and 2,4,5-T based products. Such incidents resulting from both accidents and routine occupational exposures have been reported from several countries.²

The first reported industrial accident involving exposure to TCDD occurred in 1949 at the Monsanto Company plant in Nitro, West Virginia. A total of 122 employees developed symptoms of chloracne following a trichlorophenol (TCP) process accident. An undetermined number of other employees developed symptoms of chloracne resulting from exposure to the regular operations concerned with 2,4,5-T production over the period 1948-1969.

Between 1949 and 1953, Ashe and Suskind^{3,4} examined thirty-eight Nitro plant employees with chloracne. Twelve of these had developed symptoms of chloracne directly following the 1949 TCP accident; twenty-six other chloracne cases had resulted from exposure to the regular 2,4,5-T production operations. In addition to chloracne, other signs and symptoms were observed in this group. These included severe aches in the lower extremities, fatigue, nervousness and irritability, loss or decrease of libido, dyspnea, and vertigo. These findings are consistent with those that have been reported in other industrial incidents.⁵

To examine the chronic health effects of exposure to TCDD, a mortality study of the Nitro plant employees who had developed symptoms of chloracne following the 1949 TCP accident was conducted. The study cohort was comprised of 121 of the 122 chloracne cases; one female who was living as of the endpoint of the study was excluded from analysis. At the time of the incident, it was assumed that symptoms were caused by exposure to unknown products of decomposition. From today's vantage point, these symptoms suggest exposure to TCDD. The 121-member study cohort, with a presumptive high-peak exposure to TCDD, was followed for mortality through 1978. The entire cohort was traced: thirty-two deaths were observed and eighty-nine persons were confirmed as living. Analysis indicated no excess in total mortality or in deaths from malignant neoplasms.

The study presented here examines the mortality of Nitro plant workers who were assigned to an area of TCP or 2,4,5-T production, with potential for exposure to TCDD. The mortality of these workers is examined in the context of the mortality experience of the total Nitro plant worker population.

The Monsanto Nitro plant began operations in 1922, when the Rubber Service Laboratories purchased the plant as war surplus and began production of chemicals and additives for the growing rubber industry. In 1929, Monsanto Company purchased the Nitro plant from the Rubber Service Laboratories and entered the rubber chemicals business. Over the years, the Nitro plant has diversified to where it now produces agricultural chemicals, paper chemicals, plasticizers, fine chemicals, and intermediates, in addition to rubber chemicals. The plant is situated in the Kanawha River Valley, an area containing one of the largest concentrations of chemical production facilities in the United States.

Of the many chemicals used over the years at the Nitro plant, one has an established association with the occurrence of cancer in man. Para-aminobiphenyl (PAB), used from 1941 through 1952 for use as a rubber antioxidant and dye intermediate, was shown in 1954 by Walpole et al.⁷ to induce bladder cancer in dogs. In 1955, Melick et al.⁸ confirmed the carcinogenicity of para-aminobiphenyl to man with the reporting of bladder tumors among workers exposed to this chemical at two Monsanto plants. Para-aminobiphenyl was produced at one plant and then transferred by tank car to the Nitro plant where additional processing was carried out. The minimum duration of exposure reported to have produced a bladder tumor is 133 days; the latent period has ranged from 15 to 35 years.⁹ An intensive screening program was instituted at Monsanto Company about 1955 to examine on a continuing basis, all workers exposed to this chemical. Seven deaths from bladder cancer have occurred among Nitro plant employees enrolled in this program. These seven deaths are included in the present study.

Other chemicals with known health effects produced at the Nitro plant include methylparathion and carbon disulfide. The acute effects of exposure to each of these chemicals have been described^{9,10} while the chronic effects are less well understood. Besides p-aminobiphenyl, several other rubber chemicals are of potential health concern. For all of these, there is insufficient evidence to evaluate their carcinogenicity to man. Tetramethyl thiuram disulfide is considered an animal carcinogen¹¹ and there is some evidence, although not sufficient, that N-methyl-N,4-dinitrosaniline is also an animal carcinogen.¹² For several other rubber chemicals, there is insufficient evidence to evaluate the carcinogenicity to animals. However, these chemicals have the potential for forming nitrosamines, certain of which are known animal carcinogens.¹³ Zinc dimethyl dithiocarbamate, tetramethyl thiuram disulfide and tetramethyl thiuram monosulfide have the potential to form N-nitrosodimethylamine. N-Nitrosomorpholine has been found in product samples of 2-(morpholinothio) benzothiazole and 4,4'-dithiodimorpholine (Frisone, G.J., The General Tire and Rubber Company, unpublished data).

Although several of the chemical compounds produced or used at the Nitro plant over the years have been associated with adverse health effects, no attempt has been made to relate chemical exposure to mortality with the exception of decedents exposed to the TCP or 2,4,5-T operations and potentially exposed to TCDD. As a result, the only specific hypothesis that can be tested is whether a relationship exists between potential TCDD exposure and proportional mortality, especially for malignant neoplasms. The mortality for this group is examined in addition to that of the total Nitro plant worker population.

POPULATION AND METHODS

A study cohort was developed from the Nitro plant consisting of employees active on or after January 1, 1955 with one or more years of employment on the hourly roll prior to December 31, 1977. Salaried personnel who had never worked on the hourly roll were excluded from study because many of these employees had no appreciable exposure to the plant environment and, for the most part, their exposure cannot be determined from plant records. Females and non-white males were also excluded because of their small numbers.

The cohort was assembled using government earnings reports, independent of the plant work history records. Annual earnings reports were available on a computer file from 1951 through 1977. Names and social security numbers were identified from this source. Work history records were used to supplement the earnings records. Information on race, sex, date of birth, date of hire, date of separation, and, if deceased, 2,4,5-T exposure was abstracted from these records. Ascertainment of 2,4,5-T exposure was confined to decedents only because it was too tedious to do for the entire cohort. The

information from the work history records was used to determine which names identified from the annual earnings records met the cohort entrance criteria. Employees identified from the earnings records who terminated prior to 1955 were not included in this study because work history records for all such employees were not retained prior to this date.

Exposure to 2,4,5-T was determined by assignment to a 2,4,5-T operation based on the work history records. 2,4,5-T exposure was determined for all but one decedent. Employees holding a job having plant-wide responsibilities with the potential for exposure to 2,4,5-T were, for the purposes of this study, considered to be non-exposed.

The vital status of each member of the study cohort was determined using standard follow-up techniques and ascertained as of December 31, 1977. Death certificates were coded by an independent nosologist for the underlying cause of death, according to the rules of the Eighth Revision of the International Classification of Diseases. Adapted.¹⁴

Data for the total Nitro plant study population were analyzed by the modified life-table method using the U.S. population as the standard. With this method of analysis, the age-, race-, time-, and cause-specific mortality rates for the U.S. general population are applied to the person-years lived classified by age, race, and time. A standardized mortality ratio (SMR) was calculated for 23 selected cause of death categories. Cause-specific SMR's for 15 selected cancer sites were calculated for subgroups of the total Nitro plant study population defined by date of death, age at death, and year of hire. The statistical significance of the deviation in a SMR from 100 was tested using the formula:

$$\text{standard error of SMR} = \frac{100 \sqrt{\text{no. observed deaths}}}{\text{no. expected deaths}}$$

If the observed SMR differed from 100 by 1.96 standard errors, it was regarded as significant at the 5% level. A SMR was tested for significance only when the observed number of deaths was five or greater.

Data for those deceased were also analyzed according to 2,4,5-T exposure using the proportional mortality method. In this case, the expected number of deaths is calculated on the basis of proportions of deaths observed in the U.S. general population. A proportional mortality ratio (PMR) was calculated for 23 selected cause-of-death categories. PMR's were calculated separately for those exposed to 2,4,5-T and for those not exposed. The statistical significance of the deviation of a PMR from 100 was tested by calculating the 95%

confidence interval for the PMR for a given cause k according to the formula:

$$\text{confidence interval for } PMR_k = \frac{N(\text{confidence limits for } 2 \text{ of observed deaths})}{exp_k}$$

where N = number of observed deaths for all causes

Both the standardized and proportional mortality analyses were conducted using the computer program developed by Monson.¹³ The observed mortality was compared to that of the United States white male population for the time period of study.

RESULTS

A total of 884 men were identified for study and traced for deaths through 1977. The entire cohort was successfully traced. Death certificates were obtained for all deaths. Seven hundred twenty-one (82%) were verified as living and 163 (18%) were confirmed dead by death certificates.

Tables 1-3 characterize the total Nitro plant study population by age at hire, year of hire, and length of employment. The distribution of the study population by age at hire indicates that the workers were fairly young at first hire (Table 1). Seventy-two percent of the study cohort were hired by age 30. None were hired at age 50 or above.

Table 2 shows the distribution of the study population by year of hire. The majority of workers (75.3%) were hired during the period 1940-1959, while smaller percentages of workers were hired prior to 1940 (10.8%) and after 1960 (13.9%).

An examination of the study population by length of employment indicates a fairly even distribution over the intervals less than 10 years, 10-19 years, 20-29 years, and greater than 30 years (Table 3).

Observed and expected deaths occurring during 1955-1977 among the total Nitro plant study population are shown by cause in Table 4. The SMR for all causes of death was 103 with 163 deaths observed and 158.10 expected. There were 35 deaths from malignant neoplasms with 30.92 expected, yielding a SMR of 113. Significantly elevated SMR's were seen for the categories of malignant neoplasms of the genitourinary organs and of the bladder. The SMR for bladder cancer was 989 with 9 deaths observed and 0.91 expected. This excess in bladder cancer deaths is reflected in the elevated SMR for malignant neoplasms of the genitourinary organs. A significantly elevated SMR is also seen for arteriosclerotic heart disease. There were 79 deaths from this cause with 59.40 expected (SMR = 133). The SMR for

Table 1. Distribution of Total Nitro Plant Study Population by Age at Hire

Age at Hire	Number	Percent
<20	122	13.8
20-29	518	58.6
30-39	191	21.6
40-49	53	6.0
50+	0	0.0
Total	884	100.0

Table 2. Distribution of Total Nitro Plant Study Population by Year of Hire

Year of Hire	Number	Percent
Prior to 1930	21	2.4
1930-1939	74	8.4
1940-1949	361	40.8
1950-1959	305	34.5
1960-1976	123	13.9
Total	884	100.0

Table 3. Distribution of Total Nitro Plant Study Population by Length of Employment

Length of Employment (yrs.)	Number	Percent
<10	225	25.5
10-19	213	24.1
20-29	204	23.1
30+	242	27.4
Total	884	100.1

**Table 4. Observed and Expected Number of Deaths
Standardized Mortality Ratios (SMR'S)**

Cause of Death

All causes of death.

All malignant neoplasms

Buccal cavity and pharynx

Digestive organs and peritoneum

Stomach

Liver

All other digestive organs

Respiratory system

Lung

All other respiratory organs

Skin

Genitourinary organs

Bladder

All other genitourinary organs

Lymphatic and hematopoietic tissue

Other sites

Diseases of the nervous system and sense organs

Diseases of the circulatory system

Arteriosclerotic heart disease, including CHD

All other diseases of the circulatory system

Diseases of the respiratory system

Diseases of the digestive system

All other diseases

External causes of death

Number at risk: RR4

Person-years at risk: 13968.7

4.2.05

During 1955-1977 by Cause Showing
for Total Nitro Plant Study Population

ICDA Codes

8th Rev.ObservedExpectedSMR

	163	158.10	103
140-209	35	30.92	113
140-149	0	1.03	0
150-159	4	8.65	46
151	1	1.63	61
155-156	0	0.60	0
---	3	6.42	47
160-163	14	10.51	133
162-163	14	9.91	141
---	0	0.60	0
172-173	0	0.58	0
185-189	12	3.75	320*
188	9	0.91	989*
---	3	2.84	106
200-209	1	3.15	32
---	4	3.25	123
320-389	0	1.28	0
390-458	92	82.59	111
410-413	79	59.40	133*
---	13	23.19	56*
460-519	6	9.13	66
520-577	5	8.03	62
---	5	10.46	48*
800-998	20	15.69	127

other circulatory diseases was significantly low at 56. A significant deficit was also seen for the category of all other diseases where SMR was 48 with 5 deaths observed and 10.46 expected.

Trends for malignant neoplasm deaths with calendar time are shown in Table 5. SMR's which increased consistently over the period 1955-1977 are seen for the categories of all malignant neoplasms and malignant neoplasms of the respiratory system. The SMR for all malignant neoplasms rose from 32 to 131. The SMR for malignant neoplasms of the respiratory system rose from 0 to 172 reflecting a SMR for lung cancer which increased from 0 to 181. Although based on very small numbers the SMR for malignant neoplasms of the digestive organs and peritoneum consistently decreased over time from 99 to 24. The SMR for malignant neoplasms of the genitourinary organs peaked during the period 1960-1969. This is reflected in the SMR for bladder cancer which increased from 0 in 1955-1959 to a peak of 1471 in 1960-1969 and decreased to 833 in 1970-1977.

The analysis of observed and expected deaths from malignant neoplasms by age at death revealed little in terms of consistent trends with age (Table 6). For most of the cause-of-death categories, the SMR peaked at age 45-64 rather than continuing to rise with increasing age. Bladder cancer is one category where the SMR remained high at age 65 and over.

The distribution of deaths from malignant neoplasms by year of hire is shown in Table 7. No deaths from malignant neoplasms were observed among workers hired after 1960. The SMR for all malignant neoplasms was similar for those hired prior to 1945 and for those hired in the period 1945-1959. The greatest difference in SMR's between those hired prior to 1945 and those hired from 1945-1959 occurred with bladder cancer. The SMR for bladder cancer is highest for those hired prior to 1945 with a SMR of 1111.

A subset of deaths identified from the total Nitro plant study population was studied separately. Table 8 characterizes the decedents according to 2,4,5-T exposure. Of the 163 decedents, 58 (35.6%) were considered to be exposed to 2,4,5-T based on their work history records, while 104 (63.8%) were considered to be non-exposed. The exposure of one decedent was unknown.

The results of the proportional mortality analysis by 2,4,5-T exposure classification are presented in Table 9. The proportion of cancer deaths among 2,4,5-T workers is lower than in the non-exposed group (PMR: 82 vs. 122). The PMR for lung cancer deaths is slightly higher in the exposed group (PMR: 159 vs. 117). The proportion of deaths due to bladder cancer is higher among the decedents not exposed to 2,4,5-T. There were 7 deaths from bladder cancer among these workers with 0.65 expected (PMR = 1077). The PMR for bladder cancer among decedents exposed to 2,4,5-T was 909 with 2 deaths observed and

Table 5. Observed and Expected Deaths from Malignant Neoplasms During 1955-1977 by Calendar Time Showing Standardized Mortality Ratios (SMR'S) for Total Nitro Plant Study Population

Cause of Death	Calendar Time								
	1955-1959			1960-1969			1970-1977		
	Observed	Expected	SMR	Observed	Expected	SMR	Observed	Expected	SMR
All malignant neoplasms	1	3.13	32	13	11.81	110	21	15.98	131
Buccal cavity and pharynx	0	0.11	0	0	0.41	0	0	0.50	0
Digestive organs and peritoneum	1	1.01	99	2	3.48	57	1	4.16	24
Stomach	0	0.25	0	0	0.70	0	1	0.69	145
Liver	0	0.09	0	0	0.28	0	0	0.23	0
All other digestive organs	1	0.67	149	2	2.50	80	0	3.24	0
Respiratory system	0	0.87	0	4	3.83	104	10	5.81	172
Lung	0	0.80	0	4	3.59	111	10	5.52	181
All other respiratory organs	0	0.07	0	0	0.24	0	0	0.29	0
Skin	0	0.07	0	0	0.23	0	0	0.28	0
Genitourinary organs	0	0.33	0	5	1.37	365	7	2.05	341
Bladder	0	0.09	0	5	0.34	1471*	4	0.48	833
All other genitourinary organs	0	0.24	0	0	1.03	0	3	1.57	191
Lymphatic and hematopoietic tissue	0	0.40	0	0	1.24	0	1	1.50	67
Other sites	0	0.34	0	2	1.25	160	2	1.68	119

*p < .05

Table 6. Observed and Expected Deaths from Malignant Neoplasms During 1955-1977 by Age at Death Showing Standardized Mortality Ratios (SMR'S) for Total Nitro Plant Study Population

Cause of Death	Age at Death								
	<45			45-64			65+		
	Observed	Expected	SMR	Observed	Expected	SMR	Observed	Expected	SMR
All malignant neoplasms	2	2.39	84	21	16.85	125	12	11.69	103
Buccal cavity and pharynx	0	0.06	0	0	0.67	0	0	0.31	0
Digestive organs and peritoneum	0	0.51	0	4	4.58	87	0	3.57	0
Stomach	0	0.10	0	1	0.85	118	0	0.68	0
Liver	0	0.03	0	0	0.32	0	0	0.24	0
All other digestive organs	0	0.38	0	3	3.41	88	0	2.65	0
Respiratory system	0	0.54	0	11	6.36	173	3	3.61	83
Lung	0	0.51	0	11	5.99	184	3	3.42	88
All other respiratory organs	0	0.03	0	0	0.37	0	0	0.19	0
Skin	0	0.13	0	0	0.31	0	0	0.14	0
Genitourinary organs	1	0.20	500	3	1.43	210	8	2.12	377*
Bladder	1	0.02	5000	2	0.39	513	6	0.50	1200*
All other genitourinary organs	0	0.18	0	1	1.04	96	2	1.62	123
Lymphatic and hematopoietic tissue	0	0.55	0	1	1.60	63	0	1.00	0
Other sites	1	0.40	250	2	1.90	105	1	0.94	106
*p < .05									

Table 7. Observed and Expected Deaths from Malignant Neoplasms During 1955-1977 by Year of Hire Showing Standardized Mortality Ratios (SMR'S) for Total Nitro Plant Study Population

Cause of Death	Observed	Expected	SMR	Observed	Expected	SMR	Observed	Expected	SMR
All malignant neoplasms	25	21.30	117	10	8.63	116	0	0.99	0
Buccal cavity and pharynx	0	0.70	0	0	0.31	0	0	0.03	0
Digestive organs and peritoneum	2	6.27	32	2	2.19	91	0	0.19	0
Stomach	0	1.21	0	1	0.39	256	0	0.03	0
Liver	0	0.45	0	0	0.14	0	0	0.01	0
All other digestive organs	2	4.61	43	1	1.66	60	0	0.15	0
Respiratory system	10	7.14	140	4	3.09	129	0	0.27	0
Lung	10	6.73	149	4	2.93	137	0	0.26	0
All other respiratory organs	0	0.41	0	0	0.16	0	0	0.01	0
Skin	0	0.31	0	0	0.22	0	0	0.05	0
Genitourinary organs	9	2.90	310*	3	0.76	395	0	0.09	0
Bladder	8	0.72	1111*	1	0.18	556	0	0.01	0
All other genitourinary organs	1	2.18	46	2	0.58	345	0	0.08	0
Lymphatic and hematopoietic tissue	1	1.95	51	0	1.00	0	0	0.20	0
Other sites	3	2.03	148	1	1.06	94	0	0.16	0

*p < .05

Table 8. 2,4,5-T Exposure Classification for Decedents During 1955-1977 Among Total Nitro Plant Study Population

2,4,5-T Exposure Classification	Number of Deaths	Percent
Exposed	58	35.6
Non-exposed	104	63.8
Unknown	1	0.6
Total	163	100.0

Table 9. Observed and Expected Number of Deaths During 1955-1977 by Cause and 2,4,5-T Exposure Category Showing Proportional Mortality Ratios (PMR'S)

Cause of Death	2,4,5-T Exposure Category					
	Exposed			Non-exposed		
	Observed	Expected	PMR	Observed	Expected	PMR
All malignant neoplasms	9	10.94	82	25	20.43	122
Buccal cavity and pharynx	0	0.38	0	0	0.64	0
Digestive organs and peritoneum	0	2.80	0	3	5.74	52
Stomach	0	0.52	0	0	1.06	0
Liver	0	0.19	0	0	0.39	0
All other digestive organs	0	2.09	0	3	4.29	70
Respiratory system	6	3.78	159	8	6.81	117
Lung	6	3.57	168	8	6.42	125
All other respiratory organs	0	0.21	0	0	0.39	0
Skin	0	0.29	0	0	0.35	0
Genitourinary organs	2	0.96	208	10	2.70	370*
Bladder	2	0.22	909	7	0.65	1077*
All other genitourinary organs	0	0.74	0	3	2.05	146
Lymphatic and hematopoietic tissue	0	1.35	0	1	2.07	48
Other sites	1	1.38	72	3	2.12	142
Diseases of the nervous system and sense organs	0	0.61	0	0	0.83	0
Diseases of the circulatory system	31	26.48	117	61	55.34	110
Arteriosclerotic heart disease, including CHD	27	19.72	137	52	39.68	131*
All other diseases of the circulatory system	4	6.76	59	9	15.66	57
Diseases of the respiratory system	2	2.67	75	4	6.49	62
Diseases of the digestive system	1	3.70	27	4	4.93	81
All other diseases	3	4.31	70	2	6.70	30
External causes of death	12	9.29	129	8	9.28	86
Total number of deaths:	58	58.00		104	104.00	

*p < .05

0.22 expected. PMR's for both exposure groups are quite similar for diseases of circulatory and respiratory system. Slight differences appear in the PMR's between the two groups for diseases of the digestive system and all other diseases. However, the PMR's for both groups are quite low. The PMR for external causes of death is slightly higher in the exposed group (PMR: 129 vs. 86).

A listing of the cancer deaths among the 2,4,5-T exposed is given in Table 10. Table 11 listed the cancer deaths among the non-exposed group.

DISCUSSION

The observation made many years ago of an apparent excess in bladder cancer among Nitro plant workers was confirmed and quantified in the mortality analysis of the total Nitro plant population presented here. The SMR for bladder cancer was 989 and was the only statistically significant SMR among those for malignant neoplasms. The excess in mortality is not seen until 1960. The SMR peaked in the 1960's and declined somewhat in the 1970's. The excess also appeared to be clustered in those decedents aged 65 years and older at death and in those hired prior to 1945. This would suggest that we should see a further decline in the SMR for bladder cancer over time.

Although not statistically significant, the SMR for lung cancer appears to be elevated. The SMR increased with calendar time and was highest in those hired prior to 1945. The elevation appears to be clustered in those aged 45-64 years of age at death (SMR = 184) and does not show a gradient with age. Further analyses to evaluate trends in lung cancer deaths as they relate to occupation cannot be carried out due to limitations in the data collected in this study.

The SMR for diseases of the circulatory system was elevated at 111. This is most likely a reflection of the higher mortality from heart disease which has been observed for Charleston, West Virginia and Kanawha County, West Virginia (unpublished data, Neas LM, 1979 and Enterline PE, 1979). For the total Nitro plant study population, there was a statistically significant excess in deaths from arteriosclerotic heart disease and a deficit in deaths from other circulatory diseases. This variation in the distribution of deaths from that of the U.S. may be due to risk factor or medical care differences in the plant population and the local area. These may include differences in smoking habits, the availability and use of medical services and the specificity of diagnoses.

The proportional mortality analysis of decedents by 2,4,5-T exposure classification indicated no unusual patterns of mortality in the 2,4,5-T exposed. The proportional mortality ratio (PMR for malignant neoplasms was low (PMR = 82) in the exposed group. Lung cancer was the only site among the malignant neoplasms which was somewhat higher in the exposed group.

Table 10. Deaths Due to Malignant Neoplasms Among
Nitro Plant Workers Exposed to 2,4,5-T

Year of Birth	Year of Hire	Year of 1st Exposure	Year of Term.	Year of Death	Smoking History*	Cause of Death as Given on Death Certificate
1917	1946	1951	1972	1972	Cigarettes	Carcinoma left lung with metastases (162.1)
1911	1948	1955	1972	1972	Cigarettes	Metastatic carcinoma of the lung (162.1)
1916	1946	1959	1968	1968	Cigarettes	Bronchiogenic carcinoma of right upper lobe (162.1)
1901	1944	1956	1963	1973	Cigarettes	Carcinoma lung with metastases (162.1)
1911	1941	1948	1971	1975	Cigarettes	Bronchiogenic carcinoma with cerebral metastases (162.1)
1922	1945	1948	1972	1973	Non-smoker	Bronchiogenic carcinoma with metastases (162.1)
1923	1946	1950	1972	1972	Cigarettes	Generalized liposarcoma (171.9)
1902	1922	1948	1966	1966	Non-smoker	Metastatic carcinoma urinary bladder (188.0)**
1910	1944	1948	1968	1968	Non-smoker	Carcinoma of the urinary bladder (188.0)**

* Obtained by interview with former coworkers of decedents.

** Included on the Nitro plant PAB roster.

Table 11. Deaths Due to Malignant Neoplasms Among
Nitro Plant Workers Not Exposed to 2,4,5-T

Year of Birth	Year of Hire	Year of Termin.	Year of Death	Smoking History*	Cause of Death as Given on Death Certificate
1911	1945	1966	1968	Cigarettes	Carcinoma of colon (153.8)
1904	1935	1957	1957	Cigarettes	Carcinoma of liver (157.9)
1899	1929	1959	1960	Pipe	Intraperitoneal carcinoma (158.9)
1905	1944	1970	1972	Cigarettes	Carcinoma of lung (162.1)
1909	1943	1962	1962	Cigarettes	Carcinoma of left lung (162.1)
1910	1927	1966	1970	Cigarettes	Pulmonary carcinoma (162.1)
1912	1944	1965	1965	Cigarettes	Carcinoma of apex of right lung (162.1)
1915	1937	1977	1977	Cigarettes	Carcinoma of lung (162.1)
1915	1939	1969	1970	Cigarettes	Carcinoma of lungs (162.1)
1894	1944	1960	1964	Non-smoker	Carcinoma of lung (162.1)
1912	1937	1973	1974	Cigarettes	Carcinoma of lung (162.1)
1919	1946	1963	1964	Cigarettes	Carcinoma of urinary bladder (188.0)**
1901	1933	1962	1977	Cigarettes	Carcinoma of bladder (188.0)**
1897	1941	1962	1965	Cigarettes	Carcinoma of urinary bladder (188.0)**
1898	1933	1962	1965	Smoked years ago	Carcinoma of urinary bladder (188.0)**
1905	1943	1971	1975	Cigarettes	Carcinoma of bladder (188.0)
1898	1943	1963	1970	Cigarettes	Bladder tumor (188.0)**
1888	1944	1956	1970	Unknown	Carcinoma of bladder (188.0)
1905	1933	1969	1977	Cigars	Prostatic carcinoma (185.0)
1906	1946	1968	1977	Cigarettes	Carcinoma of prostate (185.0)
1925	1945	1973	1974	Smoked years ago	Carcinoma of prostate (185.0)
1919	1943	1972	1973	Cigarettes	Hodgkin's Disease (201.0)
1901	1941	1964	1965	Cigars	Osteosarcoma arising from left arm (170.4)
1901	1943	1966	1977	Cigarettes	Carcinoma of liver & pancreas (197.8)
1922	1944	1964	1964	Cigarettes	Adenocarcinoma (199.0)

* Obtained by interview with former coworkers of decedents.

** Included on the Nitro plant PAR roster.

The PMR analysis is limited in that an assessment of the total force of mortality cannot be made. The cause-specific PMR's only approximate what an SMR analysis would have produced.¹⁶ The PMR analysis presented here estimates the cause-specific risks associated with 2,4,5-T exposure and potential TCDD exposure.

It is interesting to compare the results of this study of Nitro plant workers potentially exposed to TCDD with the results of the study of Nitro workers involved in the 1949 TCP accident. The workers involved in that incident had presumed TCDD exposure as evidenced by chloracne. The results of the two studies are similar in that neither shows an excess in deaths from any site among malignant neoplasms.

A recent study of Ott et al.¹⁷ found no excess in total mortality or in deaths from malignant neoplasms among workers exposed to 2,3,7,8-TCDD. These workers were probably exposed to very low levels of TCDD since no cases of chloracne were observed. Other studies of workers who developed chloracne resulting from TCDD exposure have been conducted and have been reviewed.⁶ At the present time, data from these various studies do not constitute corroborative evidence of a cancer risk emanating from any particular cancer site.

REFERENCES

1. Greig, J.B.: The toxicology of 2,3,7,8-tetrachlorodibenzo-p-dioxin and its structural analogues. Ann. Occup. Hyg. 22: 411-420, 1979.
2. International Agency for Research on Cancer: Long-term hazard of polychlorinated dibenzodioxins and polychlorinated dibenzofurans. IARC Internal Technical Report No. 78/001. Lyon: IARC, 1978.
3. Ashe, W.F. and Suskind, R.R.: Reports on chloracne cases, Monsanto Chemical Company, Nitro, West Virginia. Reports of the Kettering Laboratory, December 1949 and April 1950.
4. Suskind, R.R.: A clinical and environmental survey, Monsanto Chemical Company, Nitro, West Virginia. Report of the Kettering Laboratory, July 1953.
5. International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Vol. 15. Some Fumigants, the Herbicides 2,4-D and 2,4,5-T, Chlorinated Dibenzodioxins and Miscellaneous Industrial Chemicals. Lyon: IARC, 1977.
6. Zack, J.A. and Suskind, R.R.: The mortality experience of workers exposed to tetrachlorodibenzodioxin in trichlorophenol processing accident. J. Occup. Med. 22:11-14, 1980.
7. Walpole, A.L., Williams, M.H., and Roberts, D.C.: Tumours of urinary bladder in dogs after ingestion of 4-aminodiphenyl. Brit. J. Industr. Med. 11:105-109, 1954.

8. Melick, W.F.: First reported cases of human bladder tumors due to a new carcinogen - xenylamine. J. Urol. 74:760-766, 1955
9. Melick, W.F., Naryka, J.J., and Delly, R.E.: Bladder cancer due to exposure to para-aminobiphenyl: a 17-year followup. J. Urol. 106:220-226, 1974.
10. Key, M.M.: Occupational Diseases: A Guide to Their Recognition. U. S. Department of Health, Education and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health. DHEW (NIOSH) Publication No. 77-181. Washington: U.S. Government Printing Office, 1977.
11. International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Vol. 12. Some Carbamates, Thiocarbamates, and Carbazides. Lyon: IARC, 1971.
12. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 1. Lyon: IARC, 1971.
13. Magee, P.N.: N-nitroso compounds and related carcinogens. In: Searle, C.E.(ed): Chemical Carcinogens. Monograph 176. Washington: American Chemical Society, 1976.
14. Eighth Revision, International Classification of Diseases, Adapted for Use in the United States. U.S. Department of Health, Education, and Welfare, Public Health Service, PHS Publication No. 1693. Washington: U.S. Government Printing Office, 1977.
15. Monson, R.R.: Analysis of relative survival and proportional mortality. Comput. Biomed. Res. 7:325:332, 1974.
16. Decoufle, P., Thomas, T.H., and Pickle, L.W.: Comparison of the proportionate mortality ratio and standardization mortality ratio risk measures. Am. J. Epidemiol. 111:263-269, 1980.
17. Ott, G., Holder, B.B., and Olson, R.: A mortality analysis of employees engaged in the manufacture of 2,4,5-trichlorophenoxyacetic acid. J. Occup. Med. 22:47-50, 1980.