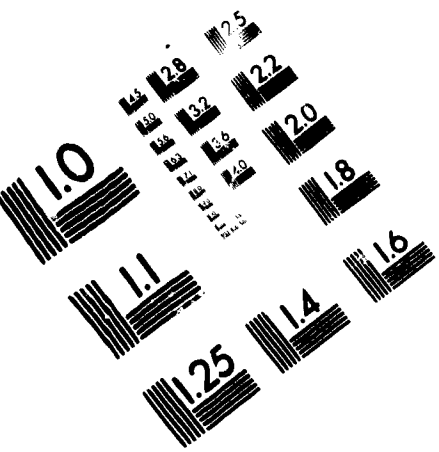

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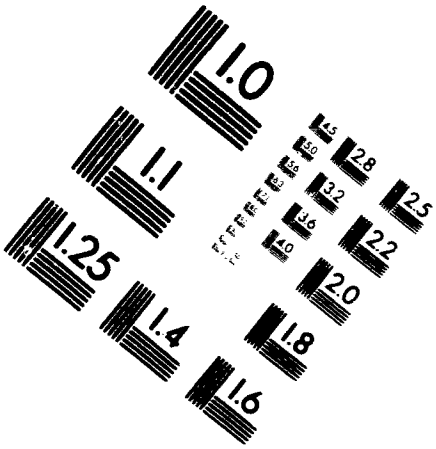

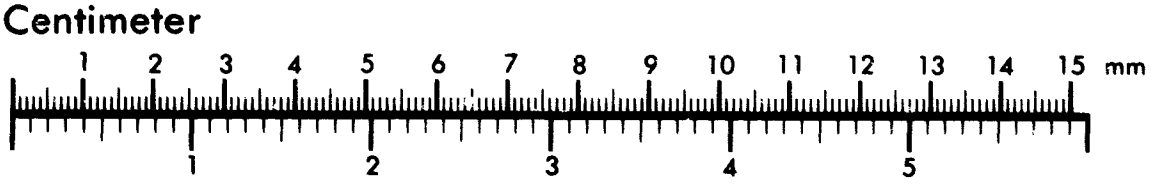

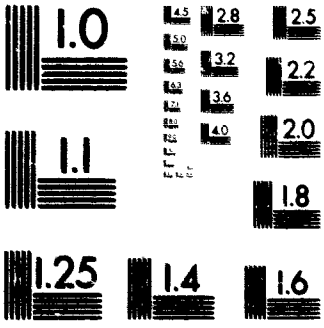

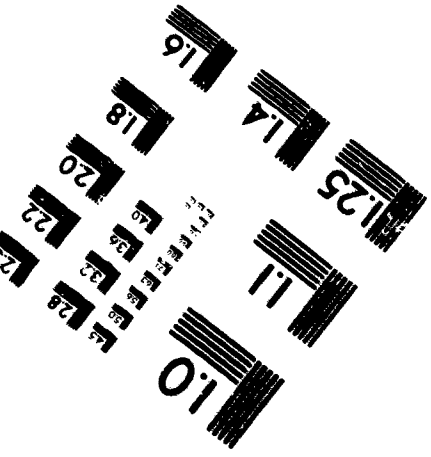

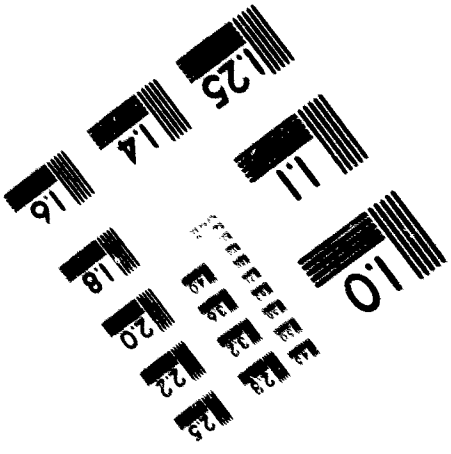

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CHEM INDUST INST OF TOXICOL

Contractor

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LETTER FROM CHEM INDUST INST OF TOXICOL TO US EPA SUBMITTING INFORMATION ON TOLUENEDIAMINES WITH ATTACHMENTS

Chemical Category

TOLUENEDIAMINES

Chemical Industry Institute of Toxicology

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Vice President, Administration and Secretary, Donald A. Hart, Ed.D.

February 24, 1983

Dr. John Helm
U.S. Environmental Protection Agency
401 M Street, S.W.
Mailstop TS-778
Washington, D.C. 20460

Dear Dr. Helm:

In accord with your request for information regarding possible rulemaking related to toluene diamine I have enclosed the following items for your consideration:

1. "Fertility of Workers Exposed to Dinitrotoluene and Toluene Diamine at Three Chemical Plants" by Richard J. Levine, R. Daniel DalCorso, and Patricia B. Blunden. In The Toxicity of Nitroaromatic Compounds ed. Douglas E. Rickert, Hemisphere Pub. Inc. (in press).

2. "The Fertility of Workers Exposed to Dinitrotoluene and Toluene Diamine at Olin Corporation, Lake Charles, Louisiana" by Richard J. Levine

3. "The Reproductive Experience of Workers Exposed to Dinitrotoluene and Toluene Diamine at BASF Wyandotte Corporation, Geismar, Louisiana" by Richard J. Levine

4. "The Reproductive Experience of Workers Exposed to Dinitrotoluene and Toluene Diamine at Rubicon Chemicals Incorporated, Geismar, Louisiana" by Richard J. Levine

5. Letters to Dr. James Hathaway, Medical Director: Chemicals, Allied Corporation August 17, 1981 and August 25, 1981.

6. Letters to Dr. Lloyd Tepper, Corporate Medical Director, Air Products & Chemicals Inc., July 9, 1981 and March 16, 1982.

I hope that these will be of value to you in your deliberations.

Yours truly,

Richard J. Levine, M.D.
Chief, Epidemiology

cc: Dr. Robert A. Neal
Dr. James E. Gibson
Dr. Donald A. Hart

FERTILITY OF WORKERS EXPOSED TO DINITROTOLUENE AND TOLUENE DIAMINE AT THREE CHEMICAL PLANTS

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Department of Epidemiology

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INTRODUCTION

Exposure to dinitrotoluene (DNT) and toluene diamine (TDA) in the workplace has been suspected to impair spermatogenesis and to increase the risk that workers' wives may undergo spontaneous abortion.[1] While little is known about the potential for TDA to affect reproduction in laboratory animals, DNT administered in doses far exceeding occupational exposures has been shown to impair spermatogenesis and cause testicular atrophy and reduced fertility.[2-6] On the other hand, dominant lethal mutations, increases in the proportion of non-viable conceptions which result from exposure of male animals have not been observed.[5,6] Because of concern that chemical exposures might be affecting reproduction, the managements of three U. S. chemical plants producing DNT and TDA requested CIIT to evaluate the reproductive experience of exposed employees.

BACKGROUND AND METHODS

Plant A manufactures only DNT and TDA. Since job titles did not distinguish between these manufacturing processes, identification of exposures was made as follows: Employees were assumed to have had no exposure to either chemical at the plant prior to May 1973, when DNT was first produced. After that date, the reproductive experience of persons working at jobs with little or no potential for exposure was considered to be unexposed. Between May 1973 and April 1976, when TDA production began, there was potential for exposure to DNT, but not to TDA. From April 1976 on there was the possibility for exposure to both DNT and TDA.

A few employees of Plant A had previously worked at another plant - Plant X - where they may have been exposed to DNT. In view of the fact

that those who had worked at Plant X were not a representative sample of Plant X employees, little should be inferred from their experience about the effects of Plant X exposures. In assessing the effects of exposure on fertility, therefore, experience related to exposure at Plant X has been excluded.

A variety of chemicals are produced at Plant B. These include toluene diisocyanate for which the plant makes the intermediates DNT and TDA. Production jobs are assigned by manufacturing process, which can be identified from job titles. The DNT and TDA processes are housed in separate buildings. In the DNT process there is no possibility for exposure to TDA. Opportunity for exposure to DNT in the TDA process is considered slight.

Plant C is organized by production areas and not by individual products or manufacturing processes. Employees are assigned to an area and rotate through all activities in the area according to a two-week or a one-month rotation schedule. The only significant exposures to DNT occur in the nitrations area ("DNT+"), which includes offsites (loading methylene diphenyl diisocyanate; receiving benzene, toluene, ammonia, and other raw materials), sulfuric acid concentration, and the manufacture of nitric acid, DNT, and nitrobenzene. Significant exposures to TDA occur only in the reductions area ("TDA+"), where TDA, aniline, and diphenylamine are produced.

Fertility during first and last marriages of female employees or the wives of male employees was analyzed according to the method of Levine et al.[7] Unmarried experience and married experience following permanent separation (i.e. observed or expected births occurring within nine months of marriage or

more than nine months after permanent separation) was excluded from analysis.

At Plant A dates of hire were obtained from personnel records, but job titles and dates of job changes were provided by the employees. Most employees did not change jobs; and when a job change was made, it usually was from one exposed (or unexposed) job to another. Inaccuracies of dates of job changes, therefore, are likely to influence only slightly the overall assessment of the effects of exposure on fertility. Job titles and dates comprising in-plant occupational histories at Plants B and C were provided by the plant personnel offices and verified with employees. At each plant a corporate industrial hygienist assessed the potential for exposure of all jobs.

Interviews at Plant A were obtained in two rounds. During 1979 questionnaires were administered to 137 of 152 permanent* employees (90 percent). The following year 91 employees were interviewed, 84 of whom were interviewed for the second time using follow-up questionnaires. Data from both sets of interviews were pooled. In 1981 all permanent* employees of Plants B and C whose jobs had ever taken them into the production areas of the plants on a regular basis were invited to participate in questionnaire surveys. Of 221 eligible persons at Plant B, 207 (94 percent) were interviewed; at Plant C 235 were interviewed from among 268 eligible (88 percent). Most persons not interviewed were unavailable due to vacation or medical absence rather than refusal to participate.

*Since adequate job histories were not available for persons employed by contractors, such individuals were not included in the study.

RESULTS

Results of the fertility analyses are presented in Tables 1-4. Observed and expected births and the resulting ratio or standardized fertility ratio (SFR) are recorded for different portions of group reproductive experience. Pre-employment fertility is set forth in the pair of numerical columns at farthest left. Other pairs of columns display post-employment fertility according to whether there were 1) little or no opportunity for exposure ("No" or "None") -- e.g. layoff or other absence, administrative and certain technical jobs, or any job prior to the start of chemicals production; 2) opportunity for exposures to DNT or TDA or both; 3) for multiple exposures not limited to one production area, as with various maintenance, laboratory, and technical positions; or 4) "Other" exposures, referring to the experience of individuals assigned to work in discrete production areas without potential for exposure to DNT or TDA.

In order to check for the possible influence of socioeconomic status on fertility, persons who had ever been hourly employees were designated "hourly"; similarly, those who had ever been salaried were "salaried". Persons who had been both hourly and salaried were denoted "hourly/salaried" and were also included in "hourly" and "salaried" categories. Pre-employment fertility and weighted mean age of wives before plant employment were similar for hourly and salaried persons. Since these designations of themselves did not appear to affect fertility prior to employment at the plants, they were not considered in evaluating the effects of exposure.

The change in fertility with exposure (Table 5) is denoted by theta (θ) and computed as the ratio of SFRs during and in the absence of exposure

(SFR exposed/SFR unexposed). SFRs based upon fewer than five expected births are unstable and have been disregarded.

Exposure-related fertility among non-white male employees, those with Spanish surnames, and female employees was insufficient to analyze.

Plant A

The relationship of fertility to exposure at Plant A is described in Tables 1 and 5. Since it was not possible to develop stable estimates of fertility at risk from DNT exposure alone, DNT-related fertility of all male employees was combined with fertility associated with DNT or TDA exposures. This results in θ = 1.05 (22/11.0 / 126/66.3) with 90% confidence limits 0.69 and 1.56. A 60% reduction in fertility (θ = 0.40) could have been detected at the p = 0.05 level of significance with a power of 0.9.

Plant B

Fertility of Plant B employees is described in Tables 2, 3, and 5. Table 2 presents fertility at all parity levels ("aggregate fertility") by exposure; Table 3, parity-specific fertility. In analyzing the effects of exposure on fertility, fertility related to the pre-employment period and to post-employment exposures "None" and "Other" has been used as the baseline. For all men, estimates of theta for DNT, TDA, and multiple exposure, which may include exposure to DNT and TDA, are 0.97 (11/6.2 / 410/225.3), 0.80 (11/7.6 / 410/225.3), and 0.87 (90/56.8 / 410/225.3), respectively.

Changes in fertility during DNT and TDA manufacturing can also be estimated by considering only the baseline experience of persons who have

worked in these areas. For DNT-exposed men, theta related to the DNT manufacturing process is 1.02 (11/6.2 / 52/29.8); for TDA-exposed men, theta related to TDA manufacturing is 0.87 (11/7.6 / 55/33.1). Using only fertility at parities 1 or higher (cf. parity 1+ fertility in Table 3) among all men, theta is 1.41 (11/6.1 / 252/196.7) for DNT, 0.89 (8/7.0 / 252/196.7) for TDA, and 1.06 (74/54.4 / 252/196.7) for multiple exposures; among TDA-exposed men, theta related to TDA exposure is 1.17 (8/7.0 / 27/27.7). The baseline fertility of exposed and unexposed persons did not differ significantly.

None of the estimates of theta is significantly different from unity. Among all men, a 70% reduction in fertility during either DNT or TDA exposure and a 30% reduction during multiple exposure could have been detected at the $p = 0.05$ level of significance with a power of 0.9.

Plant C

The fertility of Plant C employees by exposure is presented in Tables 4 and 5. Using fertility related to the pre-employment period and to post-employment exposures "None" and "Other" as the baseline, estimates of theta for all men at risk from DNT+, TDA+, and multiple exposure are 0.94 (17/8.5 / 294/138.4), 0.95 (32/15.9 / 294/138.4), and 0.94 (30/15.0 / 294/138.4), respectively. Among men who had ever been exposed, respective estimates for DNT+ exposure and TDA+ exposure are 1.04 (17/8.5 / 85/44.0) and 0.99 (32/15.9 / 66/32.4). Values of theta would have changed little if experience at risk from "other" post-employment exposures had been deleted from the baseline.

None of these estimates of theta is significantly different from unity. Among all men, a 50% reduction in fertility during TDA+ or multiple exposure and a 60% reduction during DNT+ exposure could have been detected at the $p = 0.05$ level of significance with a power of 0.9.

DISCUSSION

Estimates of the change in fertility with exposure have been determined from the experience of all men employed at the plants or from that of persons who had ever been exposed, at all parities or at parities one and greater. Use of the non-exposed experience of ever-exposed men as a baseline minimizes the concern that differences associated with exposure might have resulted from inherent differences in the fertility of exposed persons. No significant differences, however, between the fertility of exposed and unexposed persons were noted.

The analysis of aggregate fertility assumes that SFRs do not vary with female age, birth cohort, or parity, or that the distribution of these parameters is similar across exposure periods. With respect to the relationship of parity and married fertility, this assumption is false.

The relationship of parity to fertility among employees of Plant B is presented in Table 3. It can be readily discerned that the magnitude of SFRs is not constant across parity levels and declines with increasing parity. This is evident from a scrutiny of parity-specific SFRs during the preemployment period, when fertility is unlikely to be confounded by differences in environmental exposures. The greatest decrement in fertility occurs between parities 0 and 1 and may be attributed to the preponderance of nulliparous single women at parity 0 in the general population from whom birth probabilities are determined. This depresses the expected number of births at parity 0 and, since the reproductive experience of the group under study is married experience, it increases the SFR. According to the 1970 U.S. census an estimated 74 percent of never married, separated, widowed, and

divorced women between the ages of 15 - 49 were childless.[8] At higher parities, therefore, the proportion of single women in the general population - and hence the discrepancy from married experience - is greatly reduced.

Because workers are older after employment at the plant than before, their post-employment fertility is likely to contain less parity 0 experience. The corresponding U.S. general population is also older and usually includes a greater proportion of married women since the proportion married increases with age until the early thirties.[9] For these reasons SFRs at parity 0 tend to contribute less to aggregate fertility and to be smaller after employment at the plant than during the pre-employment period. This results in artifactual reduction of post-employment aggregate SFRs when compared to pre-employment fertility, a phenomenon which may be termed the "marital status artifact." A good example of the marital status artifact can be observed in Table 3. Aggregate pre-employment SFRs for all men and TDA-exposed men are greater than SFRs during TDA exposure, whereas parity-specific SFRs are almost always less.

The marital status artifact may be minimized by discarding parity 0 experience and examining only fertility at higher parities. Parity 1+ experience has been examined whenever aggregate fertility during exposure is reduced, but not otherwise. This is because, after deleting parity 0 experience, estimates of theta based upon aggregate fertility would be expected to increase.

Values of theta for the three plants have been listed by exposure in Table 5 with 90% confidence limits. None is significantly less than unity; and

all are greater than or approximately equal to unity with the possible exception of TDA exposure at Plant B. In this instance parity 1+ fertility appears somewhat diminished or enhanced, according to whether the non-exposed experience of all men or of TDA-exposed men is used as the baseline.

Power analyses estimate the probability that significant fertility reductions would have been detected. The actual probability depends greatly on sample size, which in turn is very much related to the definition of exposure. Should the definition of exposure be broadened to include more than one chemical or plant, the probability of detecting a significant reduction in fertility, given a certain level of true association, would be enhanced. In general for the situations described here, a true reduction in fertility of 50 percent or more would have been detected 90 percent of the time.

To summarize, the fertility of men employed at three U.S. chemical plants has not been reduced significantly by exposure to DNT or TDA. Actual estimates suggest that fertility may not have been reduced at all. If in fact these chemical exposures are associated with large reductions in male fertility, it is likely that fertility would have been found to be significantly reduced.

ACKNOWLEDGEMENT

The advice of Dr. Thomas B. Starr and Dr. Dragana A. Andjelkovich is gratefully acknowledged.

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Table 1

MARRIED FERTILITY BY OCCUPATIONAL EXPOSURE: PLANT A*

Group	Pre-Employment		Post-Employment									
			Plant X Exposure				Plant A Exposure					
			No		Yes		No		DNT		DNT+TDA	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
All men	123/63.3	1.94	1/1.4	0.74	6/4.9	1.22	2/1.6	1.29	2/2.0	0.99	20/9.0	2.22
White	115/60.1	1.91	1/1.4	0.74	6/4.9	1.22	2/1.5	1.33	2/1.6	1.24	17/8.0	2.14
Non-white	8/ 3.2	2.52	-----	----	-----	----	0/0.1	0.00	0/0.4	0.00	3/1.1	2.82
Spanish surname	9/ 4.0	2.24	-----	----	-----	----	0/0.1	0.00	-----	----	2/0.8	2.42
Hourly	78/41.7	1.87	1/1.0	1.01	6/4.2	1.43	0/0.2	0.00	2/2.0	0.99	20/9.0	2.23
Salaried	57/29.2	1.95	1/1.4	0.74	4/3.7	1.07	2/1.4	1.42	0/0.6	0.00	1/0.8	1.30
Hourly/salaried	12/ 7.6	1.58	1/1.0	1.01	4/3.0	1.32	0/0.0	0.00	0/0.6	0.00	1/0.7	1.36
Plant X-exposed	17/ 8.9	1.92	1/1.0	1.01	6/4.9	1.22	0/0.0	0.00	0/0.2	0.00	0/0.1	0.00
All women	24/11.9	2.01	-----	----	-----	----	0/0.3	0.00	-----	----	0/0.0	0.00

O/E - observed/expected births; SFR - standardized fertility ratio; DNT - May 1973 through April 1976, the period during which only dinitrotoluene was produced; DNT/TDA - April 1976 and thereafter, when both dinitrotoluene and toluene diamine were manufactured.

*Expected births were rounded to the nearest tenth.

Table 2

MARRIED FERTILITY BY OCCUPATIONAL EXPOSURE: PLANT B*

Group	Pre-Employment		Post-Employment									
			Exposures									
			None		DNT		TDA		Multiple		Other	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
All men	301/163.6	1.84	13/9.0	1.44	11/6.2	1.76	11/7.6	1.45	90/56.9	1.58	3[illegible]/2.7	1.82
White	294/160.6	1.83	13/9.0	1.44	11/6.2	1.76	10/7.5	1.33	90/55.8	1.58	[illegible]/52.5	1.83
Non-white	7/ 3.0	2.32	0/0.0	0.00	------	----	1/0.1	10.00	0/ 0.1	0.00	0/ 0.2	0.00
Spanish surname	5/ 1.9	2.62	0/0.1	0.00	------	----	0/0.2	0.00	1/ 1.0	1.00	3/ 2.2	1.82
Hourly	275/149.6	1.84	10/7.3	1.37	11/6.2	1.76	11/7.6	1.45	82/53.6	1.53	94/52.6	1.79
Salaried	69/ 37.3	1.85	5/4.0	1.25	1/1.2	0.83	5/3.6	1.39	2[illegible]/[illegible]	[illegible]1	21/10.2	2.06
Hourly/salaried	43/ 23.3	1.84	2/2.4	0.83	1/1.2	0.83	5/3.6	1.39	7/10.4	1.53	19/10.0	1.90
DNT-exposed	38/ 22.0	1.73	2/0.7	2.86	11/6.2	1.76	0/0.4	0.00	3/ 4.1	1.95	12/ 7.1	1.69
TDA-exposed	41/ 23.8	1.72	0/0.7	0.00	3/0.5	6.31	11/7.6	1.45	1[illegible]/ 7.6	2.24	14/ 8.6	1.63
All women	20/ 9.5	2.11	2/1.0	2.00	0/0.0	0.00	0/0.0	0.00	0/ 0.0	0.00	0/ 0.7	0.00

O/E - observed/expected births; SFR - standardized fertility ratio; DNT - the DNT manufacturing process; TDA - the TDA manufacturing process; Multiple exposures - persons who cannot be assigned to a particular area and may encounter a multiplicity of exposures, such as plantwide maintenance workers, loaders, and laboratory personnel; Other exposures - sulfuric acid concentrations, organic and inorganic waste treatment, and the following manufacturing processes: toxilic acid anhydride, maleic acid anhydride, fumaric acid, malic acid, nitrobenzene, aniline, carbon monoxide, phosgene, and toluene diisocyanate; No exposure ("None") - layoff or leave of absence, the powerhouse, and the refrigeration building.

*Expected births were rounded to the nearest tenth.

Table 3

MARRIED FERTILITY BY OCCUPATIONAL EXPOSURE AND PARITY: PLANT B MEN*

Group	Pre-Employment		Post-Employment									
			Exposures									
			None		DNT		TDA		Multiple		Other	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
All men	301/163.6	1.84	13/9.0	1.44	11/6.2	1.76	11/7.6	1.45	90/56.9	1.58	96/52.7	1.82
Parity 0	135/ 26.0	5.19	2/0.6	3.33	0/0.1	0.00	3/0.5	6.00	16/ 3.0	5.33	21/ 2.2	9.55
Parity 1	98/ 76.1	1.29	5/4.1	1.22	3/1.1	2.73	3/2.1	1.43	26/16.7	1.56	31/17.0	1.82
Parity 2	48/ 39.2	1.22	3/1.6	1.88	3/2.4	1.25	4/2.8	1.43	20/17.4	1.15	24/15.8	1.52
Parity 3	13/ 15.5	0.84	2/1.9	1.05	4/1.0	4.00	0/1.6	0.00	20/10.8	1.85	12/10.3	1.17
Parity 4+	7/ 6.9	1.01	1/0.8	1.25	1/1.6	0.63	1/0.5	2.00	8/ 9.5	0.84	8/ 7.5	1.07
Parity 1+	166/137.7	1.21	11/8.4	1.31	11/6.1	1.80	8/7.0	1.14	74/54.4	1.36	75/50.6	1.48
TDA-exposed men	41/ 23.8	1.72	0/0.7	0.00	3/0.5	6.31	11/7.6	1.45	17/ 7.6	2.24	14/ 8.6	1.63
Parity 0	22/ 4.4	5.00	0/0.0	0.00	0/0.1	0.00	3/0.5	6.00	2/ 0.4	2.50	6/ 0.7	8.57
Parity 1	13/ 12.8	1.02	0/0.4	0.00	0/0.0	0.00	3/2.1	1.43	7/ 3.1	2.26	4/ 2.5	1.60
Parity 2	6/ 5.2	1.15	0/0.0	0.00	2/0.3	6.67	4/2.8	1.43	3/ 2.2	1.36	2/ 2.7	0.74
Parity 3	0/ 1.4	0.00	0/0.2	0.00	1/0.1	10.00	0/1.6	0.00	5/ 1.0	5.00	1/ 1.5	0.67
Parity 4+	0/ 0.0	0.00	0/0.0	0.00	0/0.0	0.00	1/0.5	2.00	0/ 0.8	0.00	1/ 1.0	1.00
Parity 1+	19/ 19.4	0.98	0/0.6	0.00	3/0.4	7.50	8/7.0	1.14	15/ 7.1	2.11	8/ 7.7	1.04

O/E - observed/expected births; SFR - standardized fertility ratio; DNT - the DNT manufacturing process; TDA - the TDA manufacturing process; Multiple exposures - persons who cannot be assigned to a particular area and may encounter a multiplicity of exposures, such as plantwide maintenance workers, loaders, and laboratory personnel; Other exposures - sulfuric acid concentration, organic and inorganic waste treatment, and the following manufacturing processes: toxilic acid anhydride, maleic acid anhydride, fumaric acid, malic acid, nitrobenzene, aniline, carbon monoxide, phosgene, and toluene diisocyanate; No exposure ("None") - layoff or leave of absence, the powerhouse, and the refrigeration building.

*Expected births were rounded to the nearest tenth.

Table 4

MARRIED FERTILITY BY OCCUPATIONAL EXPOSURE: PLANT C*

Group	Pre-Employment		Post-Employment									
			Exposures									
			None		DNT+		TDA+		Multiple		Other	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
All men	252/116.8	2.16	8/2.1	3.81	17/8.5	2.00	32/15.9	2.01	38/17.9	2.12	34/19.5	1.74
White	219/100.5	2.18	8/2.1	3.81	10/5.6	1.79	30/13.6	2.21	30/15.0	2.00	28/16.0	1.77
Non-white	33/ 16.3	2.02	0/0.0	----	7/2.9	2.39	2/ 2.2	0.89	8/ 2.9	2.76	6/ 3.4	1.76
Spanish surname	3/ 0.5	5.75	0/0.0	----	0/0.2	0.00	-------	----	-------	----	0/ 0.2	0.00
Hourly	198/ 96.1	2.06	3/1.2	2.50	17/8.4	2.02	31/15.5	2.00	26/12.4	2.10	34/19.4	1.75
Salaried	97/ 41.8	2.32	7/1.5	4.67	7/3.8	1.84	11/ 6.0	1.83	26/11.9	2.18	5/ 6.6	0.76
Hourly/salaried	43/ 21.1	2.04	2/0.5	4.00	7/3.7	1.89	10/ 5.6	1.79	14/ 6.4	2.19	5/ 6.5	0.77
DNT+-exposed	75/ 37.7	1.99	1/0.4	2.50	17/8.5	2.00	7/ 3.3	2.12	5/ 2.3	2.17	9/ 5.9	1.53
TDA+-exposed	55/ 27.1	2.03	0/0.2	0.00	2/1.0	2.00	32/15.9	2.01	8/ 3.2	2.50	11/ 5.1	2.16
All women	21/ 9.2	2.28	3/1.2	2.50	0/ 0.1	0.00	0/ 0.2	0.00	0/ 0.2	0.00	0/ 0.4	0.00

O/E - observed/expected births; SFR - standardized fertility ratio; DNT+ - includes loading methylene diphenyl diisocyanate, unloading raw materials, and the following manufacturing processes: nitric acid, dinitrotoluene, and nitrobenzene; TDA+ - includes the manufacturing of toluene diamine, aniline, and diphenylamine; Multiple exposures - persons who are not assigned to a particular area and may encounter a multiplicity of exposures, such as with various maintenance, laboratory, and technical jobs; Other exposures - the following manufacturing processes: toluene diisocyanate, methylene diphenyl diisocyanate and variants, nitrobenzene, aniline, and the old nitric acid plant; No exposure ("None") - layoff or other absence, administrative and certain technical job categories.

*Expected births were rounded to the nearest tenth.

Table 5

ESTIMATES OF THETA*

Plant : Exposure	Theta (90% Confidence Limits)			
	All Parities		Parities 1+	
	All Men	Exposed Men	All Men	Exposed Men
A : DNT/TDA	1.05 (0.69,1.56)	----------	----------	----------
B : DNT	0.97 (0.54,1.63)	1.02 (0.54,1.80)	1.41 (0.78,2.36)	----------
: TDA	0.80 (0.44,1.33)	0.87 (0.46,1.54)	0.89 (0.44,1.63)	1.17 (0.54,2.37)
: Multiple	0.87 (0.71,1.06)	----------	1.06 (0.84,1.33)	----------
C : DNT+	0.94 (0.59,1.43)	1.04 (0.63,1.63)	----------	----------
: TDA+	0.95 (0.68,1.30)	0.99 (0.67,1.43)	----------	----------
: Multiple	0.94 (0.67,1.30)	----------	----------	----------

*Theta - the change in fertility with exposure (SFR exposed/SFR unexposed)

CHEMICAL INDUSTRY INSTITUTE OF TOXICOLOGY

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August 17, 1981

James Hathaway, M.D., M.P.H.
Medical Director: Chemicals
Allied Chemical Corporation
P.O. Box 1057-R
Morristown, NJ 07960

Dear Dr. Hathaway:

The analysis of fertility at Allied's Moundsville, WV plant has been completed. I expect to mail you under separate cover within the next ten days the results of the miscarriage, stillbirth, and birth defect data.

There is no evidence of a decrease in fertility related to exposure to dinitrotoluene or other agents in Building 55. Nor is there convincing evidence of a decrease in fertility related to exposure to toluene diamine or other agents in Building 52.

The study has proceeded according to the method I have presented in my recent articles and letter in the Journal of Occupational Medicine. It is based on interviews conducted by my staff towards the end of April 1981. Job titles and dates comprising in-plant occupational history were provided by the plant personnel and safety offices and were reviewed for accuracy with employees. Where there were conflicting opinions, the dates and job titles given by the employees were used in preference to those provided by plant management; however, in general, there was good agreement between management and employees about these matters.

I am grateful for the excellent response of your employees toward this study and to Mr. Higgins and Mr. Callow in particular--without their willing and knowledgeable assistance the study could not have been completed. A total of 268 persons--everyone whose job had ever taken him into the exposure areas of the plant on a regular basis--were invited to participate in the study. This included all hourly employees and 48 of 76 salaried staff. Persons who had worked only in the administrative offices were excluded from the study as were temporary or contract personnel. Interviews were obtained from 235 individuals, including five hourly employees who had worked in Buildings 52 or 55, but who had been absent during the April interviews. These were interviewed in May by telephone. All hourly employees who had ever worked in Buildings 52 (TDA) or 55 (DNT) were given the opportunity to participate. In sum 33 eligibles were not interviewed: 7 refused and 26 were absent as the result of vacation, sickness, accident, or long-term disability. Only

two persons (refused) were not interviewed from among 45 male employees who had ever worked in Building 52 (TDA); likewise, of 32 males who had ever worked in Building 55 (DNT), only one person (refused) was not interviewed. Ten participants had never been married and thus did not contribute to the analysis. The preponderance (213) of ever-married participants were white males. There were 3 non-white males and 9 females.

Pertinent results are displayed in the appended tables. The table entitled "Married Fertility: P-100" describes fertility during periods in which employees were married and not permanently separated. Observed and expected births and the resulting ratio or standardized fertility ratio (SFR) are recorded for different slices of group reproductive experience. Pre-employment fertility is set forth in the pair of numerical columns at farthest left. Five other pairs of columns display post-employment fertility according to whether there was little or no opportunity for exposure ("None")--e.g. layoff, leave of absence, Buildings 44 (power house) or 61 (refrigeration); opportunity for exposures in Buildings 55 (DNT) or 52 (TDA); for plantwide or multiple exposures (the "Multiple" column) such as might be encountered by maintenance or laboratory personnel and loaders; or "Other" exposures, referring to the experience of individuals assigned to work in discrete areas of the plant besides Buildings 55 or 52.

As I have discussed especially in my recent letter to the editor of the Journal of Occupational Medicine, there is a small artifactual tendency for married fertility after employment to be reduced in comparison with pre-employment fertility (or for no-exposure fertility, consisting of the sum of pre-employment and post-employment "None" experience, to exceed post-employment exposed fertility). This is because the U.S. general population from which expected births for the plant population are derived will contain a greater proportion of married women at older ages; and workers are indeed older after employment (exposure) than before. Plant observed fertility, on the other hand, is based only on married years. For example, the weighted average age of the wives of all males in the pre-employment category is 26 (or 27 for the total period of no exposure as defined above). Corresponding weighted average ages for post-employment exposure categories range from 32-37, thereby resulting in a six (eight) percent increase in the proportion married among the general population compared to no-exposure (pre-employment) periods. Post-employment standardized fertility ratios, therefore, would be expected to be approximately six (eight) percent lower than corresponding rates during the period of no exposure (pre-employment).

Keeping this in mind, the pattern of fertility for male employees can be interpreted. DNT or "Other" exposure-related fertility, if anything, is probably slightly higher than no-exposure or pre-employment fertility. Fertility for the post-employment exposure categories "None," "TDA," and "Multiple" is somewhat lower than expected. Within TDA-exposed males, TDA-exposure related fertility remains less than corresponding fertility during no-exposure periods. The analysis of fertility based on the table entitled "Married Fertility: P-100," however, deals with aggregate fertility during different exposure periods. It assumes that the underlying fertility of the group does not vary with female age, birth cohort, or parity or that the distribution of these parameters is similar across exposure periods. The parameter with greatest impact on fertility is parity.

The relationship of parity to fertility among P-100 males is set forth in the tables entitled "Married Fertility by Parity: P-100 Males" and "Married Fertility by Parity: P-100 TDA-Exposed Males by Degree of Exposure." From the first of these tables it can be readily discerned that fertility is not constant across parity levels and declines as parity rises. This is evident from a scrutiny of parity-specific SFRs for all males during the pre-employment period, when fertility is unlikely to be confounded by differences in environmental exposures. The greatest decrement in fertility occurs between Parity 0 and 1 and may be attributed to the preponderance of nulliparous single women in the general population depressing the expected number of births at Parity 0. At higher parities SFRs continue to decline, although at a much slower rate.

For all parities except Parity 3 parity-specific SFRs are greater during the period of TDA exposure than prior to employment at the plant. This is true whether examining the fertility of all males or only that of male employees who have been exposed to TDA. The fact that aggregate fertility prior to employment seems to exceed fertility during exposure to TDA is accounted for by the much greater contribution of Parity 0 to pre-employment fertility. Sixteen percent of all male expected births for the pre-employment period occurred at Parity 0 compared to seven percent of expected births during TDA exposure. Since Parity 0 SFRs are characteristically large, the greater contribution of this parity level to aggregate fertility during the pre-employment period increases the overall pre-employment SFR.

In order to account for differences in the contributions of various parities to aggregate fertility during exposure periods, parity-specific expected births were adjusted as follows: Post-employment fertility at no risk from exposure to DNT or TDA (exposures "None" or "Other") was used as a baseline. At each parity level the number of expected births was adjusted by multiplying by the baseline parity-specific SFR divided by the baseline SFR at Parity 2. In this way baseline SFRs at other parities were converted to the baseline SFR at Parity 2. Assuming that the factors governing the divergence of parity-specific SFRs of the baseline are the same as those operating during other exposure periods, such an adjustment would produce aggregate SFRs unencumbered by differences in the contributions of various parity levels.

The table entitled "Parity-Adjusted Married Fertility: P-100 Males" displays the results of adjusting aggregate SFRs as described. The standard against which to compare adjusted SFRs is the adjusted SFR for "No Exp. + Other Exp." (baseline). The change in fertility with exposure is denoted by θ and is simply the ratio of adjusted SFRs of a given exposure period with baseline. In all cases post-employment adjusted SFRs exceed pre-employment values, and DNT-related SFRs exceed baseline. For all males, fertility during the post-employment periods "No Exposure", "TDA Exposure", and "Multiple Exposure" is less than baseline, but differences are not statistically significant and may result from random variation. Restricting the analysis to TDA-exposed males has the advantage of examining the same persons under different conditions of exposure, but the disadvantage of smaller numbers with greater attendant instability. Adjusted fertility related to TDA exposure of TDA-exposed males is virtually identical to baseline. The 90% confidence limits on θ indicate that the data available from the plant for exposure areas of concern - DNT, TDA, and Multiple Exposure - would have been sufficient at least to detect with 90% certainty a reduction in fertility of 60 - 80 percent (θ = 0.40 - 0.20) as occurred among workers exposed to dibromochloropropane (DBCP) at a California pesticide plant.

Degree of exposure to TDA was estimated by duration of exposure and by exposure intensity designations assigned to each job title by Mr. Higgins, Manager of Safety and Environment, according to his estimation of exposure potential. Computer capability was developed to subdivide the reproductive experience of an individual, if necessary, and assign one portion to one exposure group (e.g. the first 1.5 years of TDA exposure or TDA exposure as a helper) and another portion to another exposure group (e.g. TDA exposure subsequent to the first 1.5 years or TDA exposure as a foreman). Duration of exposure categories of less than 1.5 years or greater than/equal to 1.5 years were constructed in order to subdivide TDA-related expected births equally. The following job titles were linked to exposures of lesser intensity: laborer-janitor, operator prior to November 15, 1972, unit foreman, shift foreman, acting/temporary assistant foreman. Greater intensity exposures were assigned to helper, Building 52 designated laborer, and operator on/after November 15, 1972. (Operator and helper classifications were merged into a single operator category in November 1972.)

Greater degree of exposure to TDA was associated with reduced fertility with or without parity adjustment. The reductions observed in fertility cannot be explained by differences in weighted average age of wives between exposure groups (weighted average ages 28 and 33 for less than or greater than/equal to 1.5 years exposure, respectively; 32 for both intensity of exposure groups).

Of 42 male employees who had ever worked in Building 52, only one admitted to trying for a year or more to achieve a pregnancy without success beginning during the period of TDA exposure. This compares to one of 47 male employees producing the food additives malic and fumaric acids who reported a lack of success which began during the period of exposure to these acids. Both exposure periods are of comparable size in terms of numbers of births expected: 7.6 and 7.5, for TDA and malic/fumaric acids, respectively.

Persons who had held both salaried and hourly jobs were assigned both to salaried and hourly categories and separately to the hourly/salaried group. Pre-employment fertility and weighted average ages of wives during the pre-employment period are almost identical for hourly and salaried employees. There is, therefore, no difficulty in disregarding these categories in relation to fertility.

Exposure-related fertility among female employees was insufficient for analysis.

In summary, there is no evidence of a decrease in fertility related to exposure to dinitrotoluene or other agents in Building 55; nor is there convincing evidence of a decrease in fertility related to exposure to toluene diamine or other agents in Building 52. Fertility related to TDA exposure of TDA-exposed males is virtually identical to the post-employment fertility of these individuals during periods which preclude exposure to DNT or TDA ("No Exposure" and "Other Exposure"). Post-employment fertility of all male employees during such periods exceeds TDA-related fertility; but whether this is due to random variation or reflects a biological effect of occupational exposure cannot be determined with assurance. Indeed, the possibility for variation unrelated to occupational exposure to have influenced the outcome is more likely here since the exposure groups being compared include different individuals. It should be noted that the post-employment fertility of all male employees during

periods which preclude exposure to DNT or TDA exceeds to the same extent post-employment fertility during periods lacking any chemical exposure. Moreover, the incidence of noticeable fertility problems beginning during the period of TDA exposure seems not to differ from the incidence of such problems during exposure to chemicals of no concern. Nevertheless, the suggestion of a dose-response relationship between fertility and degree of exposure in Building 52, although not statistically significant, holds open the possibility that a mild reduction in fertility related to occupational exposures in this area may have taken place.

Please let me know if you require additional information or explanation. With many thanks for your generous assistance.

Yours truly,

Richard J. Levine, M.D.
Chief of Epidemiology

cc: Dr. Robert A. Neal, President
Dr. James E. Gibson, Director of Research

MARRIED FERTILITY: P-100+

Group	Pre-Employment		Post-Employment									
			Exposures									
			None		DNT		TDA		Multiple		Other	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
All employees	321/173.1	1.85	15/9.9	1.52	11/6.2	1.76	11/7.6	1.45	90/56.9	1.58	96/52.7	1.82
All males	301/163.6	1.84	13/9.0	1.44	11/6.2	1.76	11/7.6	1.45	90/56.9	1.58	96/52.7	1.82
White	294/160.6	1.83	13/9.0	1.44	11/6.2	1.76	10/7.5	1.33	90/56.8	1.58	96/52.5	1.83
Non-white	7/ 3.0	2.32	0/0.0	0.00	------	----	1/0.1	10.00	0/ 0.1	0.00	0/ 0.2	0.00
Spanish surname	5/ 1.9	2.62	0/0.1	0.00	------	----	0/0.2	0.00	1/ 1.0	1.00	4/ 2.2	1.82
Hourly	275/149.6	1.84	10/7.3	1.37	11/6.2	1.76	11/7.6	1.45	82/53.6	1.53	94/52.6	1.79
Salaried	69/ 37.3	1.85	5/4.0	1.25	1/1.2	0.83	5/3.6	1.39	25/13.8	1.81	21/10.2	2.06
Hourly/salaried	43/ 23.3	1.84	2/2.4	0.83	1/1.2	0.83	5/3.6	1.39	17/10.4	1.63	19/10.0	1.90
TDA-exposed males	41/ 23.8	1.72	0/0.7	0.00	3/0.5	6.31	11/7.6	1.45	17/7.6	2.24	14/8.6	1.63
<1.5 years exposure							8/3.9	2.05				
≥1.5 years exposure							3/3.6	0.83				
Lesser intensity							5/2.9	1.72				
Greater intensity							6/4.6	1.30				
All females*	20/ 9.5	2.11	2/1.0	2.00	0/0.0	0.00	0/0.0	0.00	0/0.0	0.00	0/0.1	0.00

O/E - observed/expected births; SFR - standardized fertility ratio; DNT - Building 55; TDA - Building 52; Multiple exposures - persons who cannot be assigned to a particular area, such as plantwide maintenance, loaders, and laboratory personnel; Other exposures - Buildings 31, 35, 41, 42, 43, 53, 57, 63, 65, 66, 67, and SAC; No exposure - layoff or leave of absence, Buildings 44, 61

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* All females were white and hourly employees; one had been both an hourly and a salaried employee.

\+ Expected births were rounded to the nearest tenth.

MARRIED FERTILITY BY PARITY: P-100 MALES[+]

Group	Pre-Employment		Post-Employment									
			Exposures									
			None		DNT		TDA		Multiple		Other	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
All males	301/163.6	1.84	13/9.0	1.44	11/6.2	1.76	11/7.6	1.45	90/56.9	1.58	96/52.7	1.82
Parity 0	135/ 26.0	5.19	2/0.6	3.33	0/0.1	0.00	3/0.5	6.00	16/ 3.0	5.33	21/ 2.2	9.55
Parity 1	98/ 76.1	1.29	5/4.1	1.22	3/1.1	2.73	3/2.1	1.43	26/16.7	1.56	31/17.0	1.82
Parity 2	48/ 39.2	1.22	3/1.6	1.88	3/2.4	1.25	4/2.8	1.43	20/17.4	1.15	24/15.8	1.52
Parity 3	13/ 15.5	0.84	2/1.9	1.05	4/1.0	4.00	0/1.6	0.00	20/10.8	1.85	12/10.3	1.17
Parity 4+	7/ 6.9	1.01	1/0.8	1.25	1/1.6	0.63	1/0.5	2.00	8/ 9.5	0.84	8/ 7.5	1.07
TDA-exposed males	41/ 23.8	1.72	0/0.7	0.00	3/0.5	6.31	11/7.6	1.45	17/ 7.6	2.24	14/ 8.6	1.63
Parity 0	22/ 4.4	5.00	0/0.0	0.00	0/0.1	0.00	3/0.5	6.00	2/ 0.4	2.50	6/ 0.7	8.57
Parity 1	13/ 12.8	1.02	0/0.4	0.00	0/0.0	0.00	3/2.1	1.43	7/ 3.1	2.26	4/ 2.5	1.60
Parity 2	6/ 5.2	1.15	0/0.0	0.00	2/0.3	6.67	4/2.8	1.43	3/ 2.2	1.36	2/ 2.7	0.74
Parity 3	0/ 1.4	0.00	0/0.2	0.00	1/0.1	10.00	0/1.6	0.00	5/ 1.0	5.00	1/ 1.5	0.67
Parity 4+	0/ 0.0	0.00	0/0.0	0.00	0/0.0	0.00	1/0.5	2.00	0/ 0.8	0.00	1/ 1.0	1.00

O/E - observed/expected births; SFR - standardized fertility ratio; DNT - Building 55; TDA - Building 52; Multiple exposures - persons who cannot be assigned to a particular area, such as plantwide maintenance, loaders, and laboratory personnel; Other exposures - Buildings 31, 35, 41, 42, 43, 53, 57, 63, 65, 66, 67, and SAC; No exposure - layoff or leave of absence, Buildings 44, 61

+ Expected births were rounded to the nearest tenth.

TDA Exposure-related 3 MARRIED FERTILITY BY PARITY: P-100 TDA-EXPOSED MALES BY DEGREE OF EXPOSURE+

	<1.5 Yrs. Exposure		≥1.5 Yrs. Exposure		Lesser Intensity		Greater Intensity	
Group	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
Parity 0	3/0.4	7.50	0/0.1	0.00	1/0.0	----	2/0.4	5.00
Parity 1	2/1.5	1.33	1/0.6	1.67	1/0.4	2.50	2/1.7	1.18
Parity 2	2/1.2	1.67	2/1.5	1.33	2/1.1	1.82	2/1.7	1.18
Parity 3	0/0.4	0.00	0/1.3	0.00	0/1.0	0.00	0/0.7	0.00
Parity 4+	1/0.4	2.50	0/0.2	0.00	1/0.4	2.50	0/0.1	0.00

O/E - observed/expected births; SFR - standardized fertility ratio; Lesser Intensity - the following job titles: laborer-janitor, operator prior to November 15, 1972, unit foreman, shift foreman, acting/temporary assistant foreman; Greater Intensity - the following job titles: operator on and after November 15, 1972 (when operator and helper classifications were merged), helper, Building 52 designated laborer

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+ Expected births were rounded to the nearest tenth.

PARITY-ADJUSTED MARRIED FERTILITY: P-100 MALES+

Group	O/E	SFR	p-value (one-tailed)	θ	90% Confidence Limits on θ
All males					
Pre-Employment	301/277.2	1.09	----	(0.70)	----------
Post-Employment					
No Exposure	13/ 11.3	1.15	0.19	0.74	(0.43, 1.23)
DNT Exposure	11/ 6.0	1.84	0.77	1.19	(0.65, 2.03)
TDA Exposure	11/ 9.3	1.18	0.24	0.76	(0.42, 1.30)
Multiple Exposure	90/ 66.3	1.36	0.19	0.88	(0.69, 1.12)
Other Exposure	96/ 59.1	1.63	0.66	1.05	(0.82, 1.33)
No Exp. + Other Exp.	109/ 70.3	1.55	----	(1.00)	----------
TDA-exposed males					
Pre-Employment	41/ 81.2	0.51	----	(0.69)	----------
Post-Employment					
No Exposure	0/ 0.9	0.00	0.52	0.00	(0.00, 4.98)
DNT Exposure	3/ 1.5	1.95	0.97	2.64	(0.64, 8.08)
TDA Exposure	11/ 14.6	0.76	0.61	1.03	(0.48, 2.14)
<1.5 yrs. exposure	8/ 9.5	0.84	0.71	1.14	(0.49, 2.56)
≥1.5 yrs. exposure	3/ 5.1	0.59	0.50	0.80	(0.20, 2.44)
Lesser Intensity	5/ 3.2	1.57	0.96	2.13	(0.74, 5.41)
Greater Intensity	6/ 10.2	0.59	0.42	0.80	(0.30, 1.92)
Multiple Exposure	17/ 14.5	1.17	0.93	1.59	(0.83, 3.10)
Other Exposure	14/ 18.1	0.78	0.63	1.05	(0.52, 2.10)
No Exp. + Other Exp.	14/ 19.0	0.74	----	(1.00)	----------

+Designations according to preceding tables. Expected births were rounded to the nearest tenth. Within "All Male" and "TDA-Exposed Male" categories, the group Post-Employment No Exp. + Other Exp. was used as a baseline from which to adjust parity and to compute p-values, θs, and 90% confidence limits.

THE FERTILITY OF WORKERS EXPOSED TO DINITROTOLUENE AND TOLUENE DIAMINE AT OLIN CORPORATION, LAKE CHARLES, LOUISIANA

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SUMMARY

An analysis of fertility at Olin Corporation's Lake Charles, Louisiana plant has revealed no evidence for a decrease in fertility related to exposure to dinitrotoluene (DNT) and toluene diamine (TDA). The power of the study of the Lake Charles plant indicates that equivalent exposure to DNT and TDA at another chemical plant, if it were to have any affect at all, would not be expected to reduce fertility by 50 percent or more.

Exposure to dinitrotoluene (DNT) and toluene diamine (TDA) in the workplace has been suspected to impair spermatogenesis and to increase the risk that workers' wives may undergo spontaneous abortion.[1] Since DNT is used to produce TDA at their plant in Lake Charles, Louisiana, the management of Olin Corporation requested Dr. Peter Hamill, a consulting epidemiologist and adjunct professor at the University of Maryland, to evaluate the reproductive capacity of plant employees. As part of his study, Dr. Hamill invited CIIT to assess the effects of occupational exposure to DNT and TDA on fertility. That analysis is the subject of the following report.

All male employees were solicited to participate in the study of reproductive capacity, which included a detailed questionnaire, a urogenital examination, and laboratory analysis of blood hormones and semen. Of 94 men identified by management as having ever been exposed to DNT or TDA at the plant, 78 (83 percent) were enlisted to participate. An additional 125, representing a minority of other plant employees, agreed to serve as controls.

The analysis of fertility was performed according to the method of Levine et al[2-4] as modified by Starr.[5] It is based upon information obtained from fertility and occupational history portions of the study questionnaire. An example of these has been included in the appendices along with related code sheets. Job titles and dates comprising in-plant occupational histories were provided by the employees at interview. Uncertainty or inconsistency of dates was minimized by cross-checking with seniority lists and with knowledgeable persons.

Questionnaires were administered by the plant medical department during the first six months of 1981. Among the 203 persons interviewed, 20 had never married and, therefore, did not contribute to the fertility analysis. Six other persons were excluded because of possible exposure to DNT or TDA at another chemical plant; and one, on account of incomplete information.

Job titles were characterized by extent of possible exposure to DNT or TDA, according to the plant senior industrial hygienist. Persons working at jobs defined as having the potential for "high" exposure may experience measureable quantities of DNT or TDA daily. These levels are usually below consensus criteria for a safe working environment. Jobs defined as having the potential for "medium" exposure either involve daily exposure at low levels since the chemicals of concern are enclosed and measured air concentrations are extremely low or have the potential for exposure in concentrations equal to a "high" exposure job, but on an intermittent basis (as, for example, with a maintenance worker who works on a TDA pump once a month). "Low" exposure represents trace exposure. No exposure indicates that exposure to DNT or TDA is below the limits of detection and that the jobs do not require these chemicals to be handled.

Table 1 presents the intensity of possible exposure to DNT and TDA by job title and work area. It can be observed that opportunity for exposure seems greatest in TDA and TDA/TDI maintenance, followed by TDI, then west zone maintenance. Exposure to DNT is limited to the TDA area and to assistant operators in nitric acid, who may be exposed while unloading DNT from tank trucks and loading the emptied trucks with nitric acid. Maintenance personnel assigned to TDA/TDI or west zone may work in the TDA area and, therefore, have potential for DNT exposure. TDA exposure is more widespread

and can occur in TDA, TDI, TDA/TDI, and west zone; moreover, there is potential for exposure in utilities and in central zone maintenance from waste TDA used as a powerhouse fuel. TDA operators have a variable opportunity for exposure, according to whether they work in the boardroom or outside and whether they unload DNT or are involved with TDA production or the production of carbon monoxide and hydrogen gases. Similar considerations apply to operator jobs in other areas. Since operator letter designations were not given at interview, all operator jobs were designated "medium" exposure in TDA and TDI, and low exposure, in nitric acid and utilities.

The results of the fertility analysis are given in Tables 2 and 3. These tables describe fertility during first and last marriages of the current or last wives of employees, but exclude married experience after permanent separation. Observed and expected births and the resulting ratio or standardized fertility ratio (SFR) are recorded for different slices of group reproductive experience. Table 2 divides post-employment fertility by work area. Pre-employment fertility is set forth in the pair of numerical columns at farthest left. Five other pairs of columns display post-employment fertility, according to whether reproductive experience was related to work in toluene diamine (TDA), toluene diisocyanate (TDI), toluene diamine and toluene diisocyanate maintenance (TDA/TDI), west zone maintenance (TDA, TDI, hydrazine, ketazine, RF-230, T-101), or all other post-employment experience, including experience on medical leave or while terminated or on layoff, or during work in the utility pool, the medical or safety departments, or the following areas of the plant: hydrazine, ketazine, RF-230 (chlorinated polyol), T-101 (chlorinated polyol), PACE (chlorinated cyanuric acid), nitric acid, sodium nitrate, urea, ammonia, soda asn, lime, east zone maintenance, central zone main-

tenance, laboratory, utilities, stores, warehouse, and administration/tech center.

The pre-employment fertility of non-whites with less than 16 years of education was considerably lower than that of other groups, although this difference was not statistically significant (SFR = 1.01, as compared to 1.49, 1.41, and 1.56 for whites with or without a college education and non-whites with a college education, respectively). Since pre-employment fertility and mean age of wives were similar for college-educated whites and non-whites and for whites without a college education, it was decided to examine their fertility together, but to analyze the fertility of non-whites with less than 16 years of education separately.

Two cohorts were established in order to minimize error in assigning the possibility of exposure to DNT or TDA by work area. This could be due to faulty recollection of dates, exposure in areas other than TDA and TDI (nitric acid, utilities) or on jobs not assigned to a particular work area (lab analyst, industrial hygienist, safety technician), or because of actual work performed in TDA or TDI while administratively assigned to other areas - as, for example, might occur during turnarounds. The "Yes" cohort consisted of all persons who had ever worked at a job with potential for exposure to DNT or TDA as determined by the plant industrial hygienist or had answered "yes" to the question, "Do you think you have had any exposure to TDA or DNT?" The "No" cohort included all others. While for the "Yes" cohort, post-employment experience related to activities other than in TDA, TDI, TDA/TDI, or the west zone, therefore, might occasionally have involved exposure to DNT or TDA, this was unlikely for the "No" cohort; nevertheless, the "all

other" fertility of the "Yes" cohort exceeded that of the "No" cohort for both race-education groups.

Fertility related to TDA, TDI, TDA/TDI, and west zone for non-whites with less than 16 years of education exceeded fertility during the pre-employment period and during all other post-employment experience. The ratio of SFRs for "Yes" and "No" cohorts combined is 2.29 (8/3.5 / 32/32.1). For college-educated whites and non-whites and for whites without four years of college, fertility related to TDA and TDA/TDI exceeded that prior to employment at the plant and during "all other" post-employment experience, while fertility related to TDI and west zone was less. None of the differences observed for individual areas was statistically significant; moreover, the potential for exposure to the chemicals of concern in TDI and the west zone, where fertility was lower, was not so great as in TDA and TDA/TDI. The SFR of TDA, TDI, TDA/TDI, and west zone combined was 1.39 (17/12.2), almost identical to SFRs of the "Yes" cohort related to pre-employment experience (SFR = 1.43) or to all other post-employment experience (SFR = 1.35). This SFR exceeded the combined SFR related to pre-employment and "all other" post-employment experience of "yes" and "no" cohorts (205/154.3 = 1.33) by a ratio of 1.05.

A more accurate reflection of the effects of exposure to DNT and TDA is presented in Table 3. Here, rather than examining the fertility of all participants and identifying fertility related to selected work areas where exposure was highest, only the fertility of persons who had ever held a job with potential for exposure is analyzed. In so doing, exposure-related fertility is more accurately depicted because the experience of persons exposed to DNT or

TDA outside the four areas selected in Table 2 is included; moreover, pre-employment and unexposed post-employment experience provide a better comparison since the same persons are compared in the presence and absence of exposure. The average period of time spent uninterrupted in a job with potential for exposure to DNT or TDA was 3.6 years.

Exposure-related fertility (low + medium intensity) for non-whites with less than 16 years of education exceeded fertility during the pre-employment period and during all other post-employment experience. The ratio of SFRs is 2.60 (10/3.9 / 20/20.3). For college-educated whites and non-whites and whites without a college education, there was no significant difference between exposed and unexposed fertility. The ratio of exposed to unexposed SFRs is 0.94 (19/14.3 / 81/57.2), with 90% confidence interval 0.59 - 1.45. Exposure to DNT and TDA at this plant, therefore, is associated with a non-significant increase of 160 percent in the fertility of non-whites with less than 16 years of education and a non-significant decrease of 6 percent among others.

Since experienced employees may be promoted to jobs of greater responsibility and less intense exposure, employees with the greatest duration of exposure in a particular department often will have jobs which involve the least intensity of exposure. In order to assess the effects of degree of exposure properly, therefore, it is necessary to stratify exposure intensity by duration. This was accomplished by creating duration of exposure strata which divided expected births within and between exposure intensity categories of the larger race-education group so as to maximize the value of the cell with the least number of expected births. In this way strata were selected of greater than/equal to or less than 2.0 years.

Non-significant differences may be observed among the various strata. Fertility of non-whites with less than 16 years of education increases across strata with greater duration of exposure and increases or remains unchanged with greater intensity. No consistent pattern is observed for college educated persons and whites without a college education.

Due to small numbers, the discriminating power of the stratified analysis is not great. Even had no births been observed within the greater intensity or duratio cells of non-whites with less than 16 years of education, differences still would not have attained statistical significance. For the larger race-education group, however, statistically significant differences would have been noted. For increased duration of exposure, significance would have been achieved with 0 observed births in the > 2.0 years cell of either low or medium intensity strata; and for increased intensity of exposure, with 0 or 1 observed births in the medium intensity cell of the $\leq$ 2.0 year stratum. The fact that statistically significant differences were not observed in these data argues against the possibility of large reductions in the fertility of heavily exposed subgroups going undetected.

The power of the study to have detected a decrease in fertility with exposure to DNT and TDA is depicted in Figure 1. The figure describes power for college-educated persons and whites with less than a college education who have ever held a job with exposure potential. Theta represents the ratio of exposed to unexposed SFRs. It will be noted that theta of 0.5, indicating a reduction in fertility of 50 percent, would have been detected at the $p = 0.05$ level of significance with a power of 0.8. This means that equivalent exposure to DNT and TDA at another chemical plant, if it were to

have any affect at all, would not be expected to reduce fertility by 50 percent or more.

The fertility experience of employees at the Lake Charles plant can be summarized as follows: For non-whites with less than 16 years of education, fertility related to work in any of the four plant areas with greatest potential for exposure to DNT and TDA exceeded fertility prior to employment at the plant and that related to work in other plant departments or areas. Among other employees, the combined fertility associated with work in these four areas exceeded that of their remaining experience. Total exposure-related fertility of exposed non-whites with less than 16 years of education was substantially greater than fertility unrelated to exposure; while the total exposure-related fertility of other exposed employees was slightly less, a difference which lacked statistical significance. Statistically significant reductions in the fertility of exposed employees, moreover, were not observed among subgroups with greater exposure.

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Table 1

EXPOSURE INTENSITY BY JOB TITLE AND WORK AREA

Area	Exposure Intensity			
	None	Low	Medium	High
TDA	any job prior to the start of TDA production on 06-23-73	Prod. Superintendent Prod. Engineer Project Engineer B Operator	Foreman Laborer A Operator	C Operator D Operator E Operator
TDI	Shipper Packer TDI Drummer any job prior to the start of TDA production on 06-23-73	Prod. Superintendent Prod. Engineer Process Engineer Supervisor Foreman A Operator D Operator E Operator	B Operator C Operator	
TDA/TDI	any job prior to the start of TDA production on 06-23-73	Process Engineer Zone Controller Foreman Supervisors	Pipefitter Electrician Millwright Welder Boilermaker Carpenter Instrumentmen Insulator	
West Zone	any job prior to the start of TDA production on 06-23-73	all job titles	----------	
Central Zone	all other job titles any job prior to the start of use of waste TDA as a power source in July 1978	----------	Pipefitter Boilermaker	
Nitric Acid	Prod. Superintendent Prod. Engineer Foreman Operator any job prior to the start of TDA production on 06-23-73	Assistant Operator	Assistant Operator (truck loader)	
Utilities	Prod. Superintendent Prod. Engineer Day Supervisor B Operator any job prior to the start of use of waste TDA as a power source in July 1978	Shift Supervisor	A Operator C Operator	
Miscellany	all other job titles any job prior to the start of TDA production on 06-23-73	Industrial Hygienist Safety Supervisor Safety Technician	Lab Analyst	

Table 2

MARRIED FERTILITY BY WORK AREA*

Group	Pre-Employment		Post-Employment									
			Work Area									
			TDA		TDI		TDA/TDI		West Zone		All Other	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
All participants	167/122.4	1.36	6/3.7	1.62	7/4.9	1.43	8/ 3.4	2.35	4/ 3.5	1.14	70/64.1	1.09
Whites	140/ 98.1	1.43	5/2.5	2.00	4/3.1	1.29	4/ 2.5	1.60	2/ 2.6	0.77	58/51.3	1.13
≥ 16 yrs education	37/ 24.8	1.49	1/0.5	2.00	-----	----	2/ 0.5	4.00	2/ 2.6	0.77	11/10.3	1.07
< 16 yrs education	103/ 73.3	1.41	4/2.0	2.00	4/3.1	1.29	2/ 2.0	1.00	2/ 2.6	0.77	47/41.0	1.15
Non-whites	27/ 24.3	1.11	1/1.2	0.83	3/1.8	1.67	4/ 0.9	4.44	2/ 0.9	2.22	12/12.8	0.94
≥ 16 yrs education	7/ 4.5	1.56	0/0.8	0.00	-----	----	2/ 0.5	4.00	------	----	0/ 0.5	0.00
< 16 yrs education	20/ 19.8	1.01	1/0.4	2.50	3/1.8	1.67	2/ 0.4	5.00	2/ 0.9	2.22	12/12.3	0.98
All whites & non-whites w ≥ 16 yrs education	147/102.5	1.43	5/3.3	1.52	4/3.1	1.29	6/ 3.2	1.88	2/ 2.6	0.77	58/51.8	1.12
"Yes" Cohort	89/ 62.2	1.43	5/3.3	1.52	4/3.1	1.29	6/ 3.2	1.88	2/ 2.6	0.77	32/23.7	1.35
"No" Cohort	58/ 40.3	1.44	-----	----	-----	----	------	----	------	----	26/28.1	0.93
Non-whites w < 16 yrs education	20/ 19.8	1.01	1/0.4	2.50	3/1.8	1.67	2/ 0.4	5.00	2/ 0.9	2.22	12/12.3	0.98
"Yes" Cohort	16/ 15.4	1.04	1/0.4	2.50	3/1.8	1.67	2/ 0.4	5.00	2/ 0.9	2.22	11/10.6	1.04
"No" Cohort	4/ 4.4	0.91	-----	----	-----	----	------	----	------	----	1/ 1.7	0.59

O/E - observed/expected births; SFR - standardized fertility ratio; TDA - includes unloading dinitrotoluene and the manufacture of toluene diamine, carbon monoxide, and hydrogen; TDI - includes the manufacture of phosgene and toluene diisocyanate; TDA/TDI - maintenance of the TDA and TDI areas; West Zone - maintenance of the following areas: TDA, TDI, hydrazine, ketazine, RF-230, and T-101; All Other - includes experience on medical leave or while terminated or on layoff, or during work in the utility pool or the medical and safety departments or in the following areas of the plant: hydrazine, ketazine, RF-230, T-101, PACE, nitric acid, sodium nitrate, urea, ammonia, soda ash, lime, east zone maintenance, central zone maintenance, laboratory, utilities, stores, warehouse, and administration/tech center. The "All Other" category also includes experience in TDA, TDI, TDA/TDI, and West Zone prior to the start of TDA production on 06-23-73.

* Expected births were rounded to the nearest tenth.

Table 3

MARRIED FERTILITY OF EXPOSED PARTICIPANTS BY INTENSITY AND DURATION OF EXPOSURE*

Group	Pre-Employment		Post-Employment					
			Intensity of Exposures					
			None		Low		Medium	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
All exposed participants	76/ 57.1	1.33	25/20.2	1.24	10/6.6	1.52	19/11.7	1.62
≤ 2.0 years exposure					6/4.0	1.50	12/ 8.9	1.35
> 2.0 years exposure					6/4.1	1.46	7/ 4.4	1.59
All exposed whites + non-whites with ≥ 16 yrs education	61/42.4	1.44	20/14.8	1.35	7/5.2	1.35	12/ 9.1	1.32
≤ 2.0 years exposure					4/2.5	1.63	7/ 6.0	1.17
> 2.0 years exposure					3/2.8	1.08	5/ 3.2	1.56
Exposed non-whites with < 16 yrs education	15/14.7	1.02	5/ 5.6	0.89	3/1.3	2.31	7/ 2.6	2.69
≤ 2.0 years exposure					1/0.7	1.42	3/ 1.3	2.31
> 2.0 years exposure					2/0.6	3.29	4/ 1.3	3.14

* Expected births were rounded to the nearest tenth.

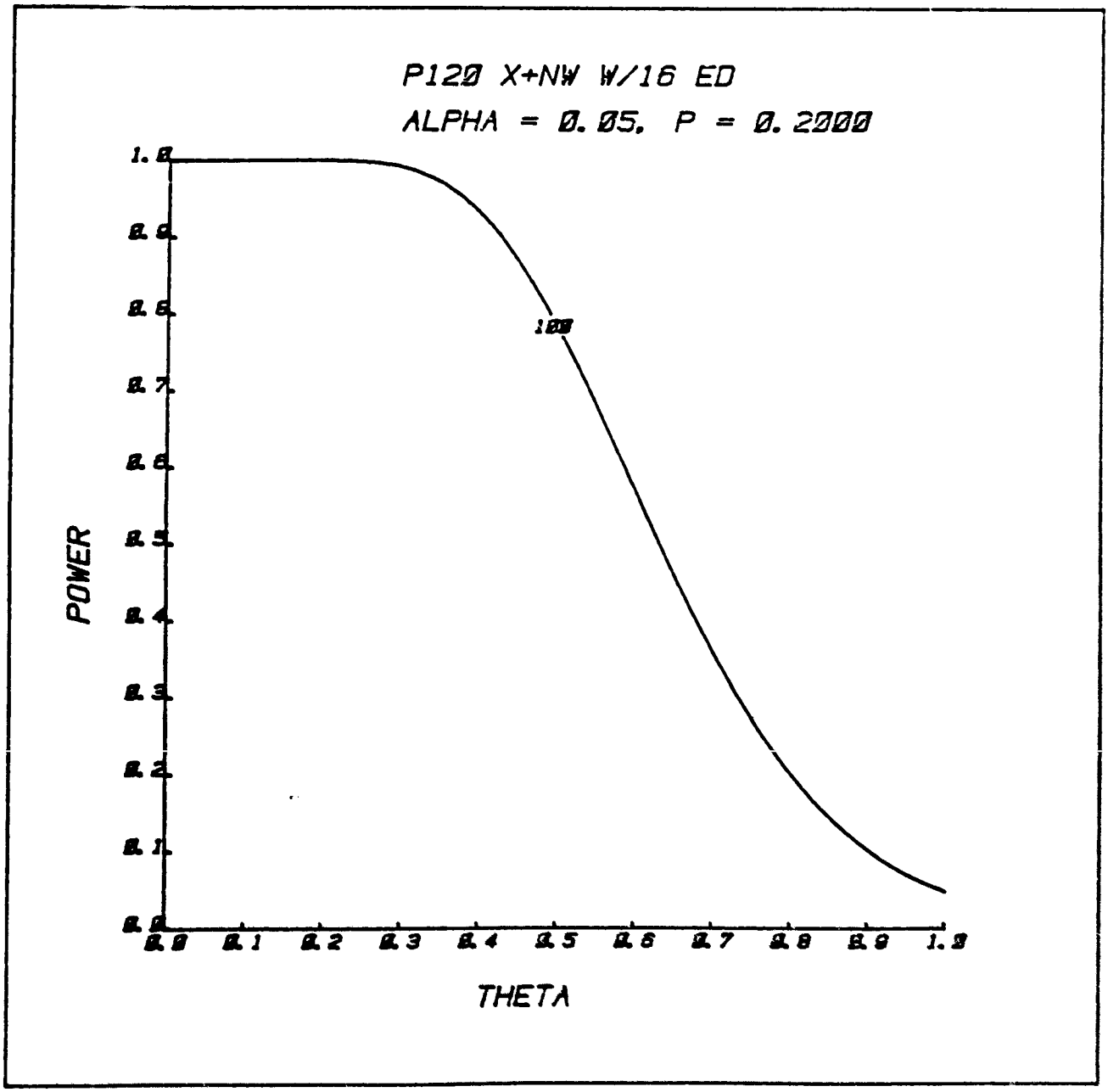

Figure 1 - Power of detecting exposure-related decreases in fertility among exposed male employees with a college education and white employees with less than four years of college. N = 100 is the total number of observed births; p = 0.2000 is the proportion of births expected to occur during the period at risk from exposure; alpha = 0.05 is the level of significance; and theta is the proportional change in fertility with exposure.

APPENDIX I

LIST OF EXPOSURE CODES FOR WHICH INDIVIDUAL FERTILITY ANALYSES ARE AVAILABLE

OLIN LAKE CHARLES

Exposure Code	Area of Exposure
001	Pre-employment
002	TDA
003	TDI
004	TDA-TDI (Maintenance)
005	Hydrazine
006	West Zone--Maintenance (R230, T101, TDA-TDI, Hyco)
007	Ketazine
008	R-230
009	T-101
010	At plant, no exposure (Administrative, Medical)
011	PACE (Chlorine)--Maintenance & Others
012	Nitric Acid
013	Lime
014	Soda Ash
015	Nitrate
016	Urea
017	Ammonia
018	Utilities (Power House)
019	Multiple exposure (Industrial Hygienist, Lab, Plantwide, Safety)
020	Central Zone--Maintenance (Utility pool, warehouse, repair work)
021	Hyco plant
022	Not used
023	TDI after TDA exposure
024	TDA-TDI--Maintenance after TDA exposure
025	Hydrazine after TDA exposure
026	West Zone--Maintenance after TDA exposure
027	Ketazine after TDA exposure
028	R-230 after TDA exposure
029	T-101 after TDA exposure
030	At plant no exposure after TDA exposure
031	PACE after TDA exposure
032	Nitric Acid after TDA exposure
033	Lime after TDA exposure
034	Soda ash after TDA exposure
035	Nitrate after TDA exposure
036	Urea after TDA exposure
037	Ammonia after TDA exposure
038	Utilities after TDA exposure
039	Multiple exposure after TDA exposure
040	East zone--Maintenance (Ammonia, Urea)
041	Not used
042	TDA exposure after TDA-TDI Maintenance
043	TDI " " " " "
044	Not used
045	Hydrazine exposure after TDA-TDI Maintenance
046	West zone Maintenance after TDA-TDI Maintenance
047	Ketazine exposure after TDA-TDI Maintenance
048	R-230 exposure after " "
049	T-101 " " " "
050	At plant no exposure after TDA-TDI Maintenance
051	PACE exposure " " "
052	Nitric Acid " " " "
053	Lime exposure " " "
054	Soda Ash " " " "
055	Nitrate " " " "

Exposure Code	Area of Exposure
056	Urea exposure after TDA-TDI Maintenance
057	Ammonia " " " "
058	Utilities " " " "
059	Multiple exposure after TDA-TDI Maintenance
060	Hydrazine/Ketazine (Maintenance)
061	Not used
062	TDA exposure after West Zone Maintenance
063	TDI " " " " "
064	TDA-TDI Maintenance after West Zone Maintenance
065	Hydrazine after West Zone Maintenance
066	Not used
067	Ketazine " " " "
068	R-230 " " " "
069	T-101 " " " "
070	At plant no exposure after West Zone Maintenance
071	PACE exposure " " " "
072	Nitric acid " " " " "
073	Lime " " " " "
074	Soda Ash " " " " "
075	Nitrate " " " " "
076	Urea " " " " "
077	Ammonia " " " " "
078	Utilities " " " " "
079	Multiple " " " " "
080	Not at plant after having worked at plant (terminated or on medical leave
099	TDA, TDI, TDA-TDI Maintenance, or West Zone Maintenance assignment prior to 6/23/73
220	Central zone after TDA exposure
420	Central zone after TDA-TDI Maintenance exposure
620	Central zone after West zone exposure
221	Hyco plant after TDA exposure
421	Hyco plant after TDA-TDI maintenance exposure
621	Hyco plant after west zone exposure
240	East zone after TDA exposure
440	East zone after TDA-TDI maintenance exposure
640	East zone after west zone exposure
260	Hydrazine/Ketazine maintenance after TDA exposure
460	Hydrazine/Ketazine maintenance after TDA-TDI exposure
660	Hydrazine/Ketazine maintenance after west zone exposure
280	Terminated or medical leave after TDA exposure
480	Terminated or medical leave after TDA-TDI maintenance exposure
680	Terminated or medical leave after west zone maintenance exposure

THE REPRODUCTIVE EXPERIENCE OF WORKERS EXPOSED TO DINITROTOLUENE AND TOLUENE DIAMINE AT BASF WYANDOTTE CORPORATION GEISMAR, LOUISIANA

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SUMMARY

Analysis of the reproductive experience of men employed at the BASF Wyandotte Geismar works has revealed little to suggest that occupational exposure to dinitrotoluene or toluene diamine may have affected reproduction adversely. Miscarriages, stillbirths, neonatal deaths, and birth defects did not aggregate with exposure to these chemicals. The fertility of non-whites lacking 16 years of education increased with exposure, while the fertility of others decreased slightly (15 percent). This reduction, while associated with exposure, is likely to have resulted from chance alone.

Exposure to dinitrotoluene (DNT) and toluene diamine (TDA) in the workplace has been suspected to impair spermatogenesis and to increase the risk that workers' wives may undergo spontaneous abortion.[1] Since DNT is used to produce TDA in the toluene diisocyanate (TDI) plant of their Geismar works, the management of BASF Wyandotte Corporation requested CIIT to evaluate the reproductive experience of TDI plant employees.

Interviews were conducted at the plant in October 1981. Twenty persons who were not available for the October interviews were reached by telephone during November. All permanent employees who had ever been assigned to the TDI plant and were currently working at the Geismar facility were included in the study. TDI assignments were generally identified from notations on personnel cards which indicated experience in TDI, urethanes, or isocyanates. TDI maintenance jobs, however, were culled from rosters of semiannual maintenance assignments kept since February 1971; and department memoranda and telephone listings were used to establish the assignments of instrument technicians.

Several persons interviewed were not included in the analysis because they did not meet the selection criteria given above. Two individuals were deleted for other reasons: one had only been assigned to the TDI plant for three days and insisted he had never actually worked there; the other reported having previously been exposed to DNT at another chemical plant. In all, 244 persons qualified for the study. Interviews were obtained from 236 (97 percent). Six persons were unable to be interviewed on account of sickness or disability; and two refused. Eighteen persons interviewed had never married, and therefore, did not contribute to the analysis. Among ever

married employees included in the study there were 208 males (166 white, 42 nonwhite) and 10 females.

The analysis of fertility was performed according to the method of Levine et al[2-4] as modified by Starr[5]. Job titles and dates comprising in-plant occupational histories for all employees were taken from personnel cards, maintenance rosters, department memoranda, and telephone listings, as noted above. It was not possible to distinguish assignments to the TDA manufacturing process area from other locations in the TDI plant; moreover, operations personnel assigned to the TDI plant would rotate through all process areas during the course of a year. All TDI plant jobs which afford potential for exposure, therefore, must be assumed to convey the possibility of exposure to DNT and TDA.

The results of the fertility analysis are given in Tables 1, 3, 4, and 5. These tables describe fertility during first and last marriages of female employees or the wives of male employees, but exclude married experience after permanent separation. Observed and expected births and the resulting ratio or standardized fertility ratio (SFR) are recorded for different slices of group reproductive experience.

In Tables 1, 4, and 5 pre-employment fertility is set forth in the pair of numerical columns at farthest left. Six other pairs of columns display post-employment fertility according to whether reproductive experience were related

to work in TDI*, glycol+, Basagran (a soybean herbicide)#, or G_2 chlorine (mercury cell process) - areas where concern has been expressed about the possibility that exposure might affect reproductive health; to potential for multiple exposures not limited to a single production area, as with various maintenance, laboratory, and salaried positions; or related to all other post-employment experience, including experience with little or no opportunity for exposure, as in the case of administrative and certain technical jobs and during layoff or other absences, and experience in the following areas of the plant: caustic, brine, polyols, butanediol, methylene bisphenyl isocyanate, utilities, offsites, and chlorine production areas without potential for mercury exposure.

Exposure-related fertility among female employees was insufficient to analyze. The following fertility analysis, therefore, refers only to male employees.

Pre-employment fertility of non-whites with less than 16 years of education was significantly lower than that of other groups (SFR = 0.96, as compared to 1.47, 1.48, and 1.67 for whites with or without a college education and non-whites with a college education, respectively). Since pre-employment fertility and mean age of wives were similar for college-educated whites and non-whites and for whites without a college education, it was decided to examine their fertility together, but to assess the fertility of non-whites with less than 16 years of education separately.

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* DNT→TDA; TDA + phosgene→TDI

\+ ethylene + oxygen→ethylene oxide→$(\text{ethylene})_{1-4}$ glycol

\# anthranilic acid, isopropyl sulfonamide, diisopropyl urea, SO_3, phosgene - all are included in the manufacturing process

A more accurate reflection of the effects of exposure can be observed in the experience of TDI-exposed or glycol-exposed individuals since only the fertility of persons who had ever held a job with potential for exposure (low, medium, or high) is analyzed. All job titles within each process area were characterized by relative extent of exposure according to the regional corporate industrial hygienist. The classification of TDI jobs is presented in Table 2. The average duration of married experience while assigned to jobs in TDI or glycol with potential for exposure was 3.7 and 2.6 years, respectively.

Fertility related to exposure in TDI or glycol for TDI-exposed or glycol-exposed non-whites with less than 16 years of education, respectively, exceeded that during the pre-employment period and during "other" post-employment experience. The ratios of SFRs are 1.55 and 3.26, for TDI exposure among TDI-exposed men and glycol exposure among glycol-exposed men, respectively (7/4.4 / 46/44.7 and 5/1.7 / 12/13.3). There were no significant differences between exposed fertility and fertility during pre-employment and "other" post-employment experience for college-educated whites and non-whites and whites without a college education. The ratio of SFRs is 0.84 for TDI exposure among TDI-exposed men (38/32.4 / 309/222.4), with 90% confidence interval 0.62 - 1.13; and 0.82 (23/19.2 / 122/83.5), with 90% confidence interval 0.54 - 1.21 for glycol exposure among glycol-exposed men. Exposure in TDI and glycol, therefore, is associated with increases of 155 and 326 percent in the fertility of non-whites with less than 16 years of education and non-significant decreases of 16 and 18 percent among others, respectively. Although reproductive experience available for analysis in Basagran and G_2 chlorine is limited, there is no evidence in these areas of exposure-related

fertility decrements; similarly, there is no decrease in fertility related to "multiple exposure, which may include exposure to chemicals used in the TDI, glycol, Basagran, or G_2 chlorine manufacturing processes.

Since experienced employees may be promoted to jobs of greater responsibility and less intense exposure, employees with the greatest duration of exposure in a particular department often will have jobs which involve the least intensity of exposure. In order to assess the effects of degree of exposure properly, therefore, it is necessary to stratify exposure intensity by duration. This was accomplished for TDI-exposed men by creating duration of exposure strata which divided expected births within and between exposure intensity categories of the larger race-education group so as to maximize the value of the cell with the least number of expected births. In this manner strata were selected of greater than / equal to or less than 1.5 years (Table 3).

Non-significant differences may be observed among the various strata, but there is no consistent pattern. Fertility tends to increase with increasing intensity of exposure in the $\leq$ 1.5 years exposure stratum. With increasing duration of exposure fertility increases slightly at low intensities, but declines at medium and high intensities. SFRs are virtually identical in the two cells affording the greatest contrast in exposure: the low intensity $\leq$ 1.5 years exposure cell and the high intensity > 1.5 years exposure cell.

Due to small numbers, the discriminating power of the stratified analysis is not great. Statistically significant differences, however, would have been noted for increased duration of exposure with 0, 0, or 4 observed births in the > 1.5 years cells of low, medium, or high intensity strata, respectively;

and for exposures of medium or high intensity as compared to low intensity, with 0 observed births in medium or high intensity cells of $\geq$ 5.1 expected births. The fact that statistically significant differences were not observed in these data argues against the possibility of large reductions in the fertility of heavily exposed subgroups going undected.

The preceding analysis of fertility assumes that the underlying fertility of the group does not vary with female age, birth cohort, or parity or that the distribution of these parameters is similar across exposure periods. The parameter with greatest impact on fertility is parity. The relationship of parity to fertility among TDI-exposed men is presented in Table 4. It can be readily discerned that fertility is not constant across parity levels and declines with increasing parity. This is evident from a scrutiny of parity-specific SFRs during the pre-employment period, when fertility is unlikely to be confounded by differences in environmental exposures. The greatest decrement in fertility occurs between Parities 0 and 1 and may be attributed to the preponderance of nulliparous single women at Parity 0 in the general population from whom birth probabilities are drawn. This depresses the expected number of births at Parity 0 and increases the SFR, since the reproductive experience of the group under study is married experience. At higher parities the proportion of single women in the general population is greatly reduced. (According to the 1970 U.S. census an estimated 74 percent of never married, separated, widowed, and divorced women between the ages of 15 - 49 were childless).[6]

Since workers are older after employment at the plant than before, post-employment fertility is likely to contain proportionately less Parity 0

experience; moreover, the corresponding U.S. general population at Parity 0 will be older and contain more married women since the proportion of married women increases with age until the early thirties. For these reasons Parity 0 SFRs tend to be smaller and to contribute less to aggregate fertility after employment at the plant than during the pre-employment period. This would result in artifactual depression of post-employment aggregate SFRs.

The "marital status artifact", as it is called, may be minimized by discarding Parity 0 fertility and examining only fertility at higher parities. Parity-specific fertility is presented in Tables 4 and 5. Among non-whites with less than 16 years of education Parity 1+ fertility related to exposure in TDI or glycol for TDI-exposed or glycol-exposed men, respectively, exceeded that during the pre-employment period and during "other" post-employment experience. The ratios of exposed to non-exposed SFRs are 1.79 and 3.93 for TDI exposure among TDI-exposed men and glycol exposure among glycol-exposed men, respectively (6/3.6 / 37/39.7 and 4/1.3 / 9/11.5). Among college-educated whites and non-whites and whites without a college education the ratio of exposed to non-exposed SFRs for TDI exposure among TDI-exposed men is 0.85 (24/27.4 / 199/192.8), with 90% confidence interval 0.57 - 1.22; and for glycol exposure among glycol-exposed men, 0.92 (18/17.8 / 79/72.2) with 90% confidence interval 0.57 - 1.44. The best estimates of exposure-related fertility, therefore, indicate increases in TDI and glycol of 179 and 393 percent, respectively, for non-whites with less than 16 years of education and non-significant decreases of 15 and 8 percent among others.

The power of the study to have detected a decrease in fertility related to exposures in TDI is depicted in Figure 1. The figure describes power for

college-educated persons and whites with less than a college education who have ever held a TDI job with exposure potential. Theta represents the ratio of exposed to unexposed (pre-employment + post-employment "other") SFRs. It will be noted that theta of 0.5, indicating a reduction in fertility of 50 percent, would have been detected at the $p = 0.05$ level of significance with a power of 0.9. This means that equivalent exposures at another chemical plant or at this plant in the future would not be expected to reduce fertility by 50 percent or more, if indeed there were to be any effect on fertility at all.

Information about abnormalities or birth defects was elicited from the questions "Did any of your wife's children have an abnormality or defect?" and "What was the abnormality or defect?" The questions did not require the informant to decide if abnormalities or defects had been present at birth since problems first noted years later might not have been identified as resulting from birth defects. Neonatal deaths were detected from responses to the questions: "Are all of your wife's children living?" and "When did he/she die?" The queries "Has your wife ever had a miscarriage or a stiliborn child?" followed by "When was the (miscarriage or stillbirth)?" and "How many months pregnant was she at the time?" were used to establish and describe these events.

Inquiries were specifically directed at pregnancies terminated by medical or surgical means which did not result in a live birth - e.g. tubal pregnancies, elective induced abortions, and intrauterine fetal deaths where labor was induced by a physician. Such pregnancy outcomes may or may not have been included in responses to questions on miscarriages and stillbirths; however, the frequency of these events is not expected to differ with chemical exposure.

Four pregnancies were reported to have been terminated by medical or surgical means. Three were conceived out of wedlock (before employment at the plant) and, therefore, do not contribute to the analysis of married experience. Marital and exposure status of the other such pregnancy was not indicated.

Data on abnormalities and defects in liveborn offspring of the wives of male employees have been summarized in Table 6. There are no significant aggregations of abnormalities or defects with chemical exposure; nor are there two or more cases of a single well-defined birth defect occurring within any one exposure category.

The distribution by exposure of miscarriages, stillbirths, neonatal deaths and live births conceived in wedlock by the wives of male employees has been enumerated in Table 7. The number of reported pregnancies at risk is probably somewhat less than the true figure. This is because pregnancies conceived within nine months of the date of interview that result in miscarriages, stillbirths, or neonatal deaths (the majority of whom have been prematurely born) are more likely to conclude prior to interview than those which result in the birth of living infants.

For purposes of analysis miscarriages, stillbirths, and neonatal deaths have been grouped together. This arrangement makes good sense if one considers that the most likely hypothesis to explain an effect on the male leading to an adverse reproductive outcome besides diminished capacity to achieve conception would involve chromosomal damage or a genetic mutation. Such an event could lead to a defect of the fetus or placenta, which if severe enough might result in a spontaneous abortion, a stillbirth, or a neonatal

death. One can easily discern in Table 4 that for all males there is no significant clustering of adverse reproductive outcomes with TDI or glycol exposure. This becomes even more evident after excluding the reproductive experience of habitual aborters, defined as women for whom three consecutive pregnancies have resulted in miscarriage, stillbirth, or neonatal death due to prematurity. These women are more likely to have constitutional abnormalities, which can account for their adverse reproductive outcomes.

The following summarizes the reproductive experience of men who may have been exposed to DNT or TDA during work at the TDI plant of the BASF Wyandotte Geismar works: There was no evidence of an abnormal aggregation of miscarriages, stillbirths, neonatal deaths, or birth defects with exposure to these chemicals. Among whites and college-educated non-whites, exposure-related fertility did decrease to a small extent (15 percent). The reduction, while associated with exposure, is unlikely to have resulted from it because of these reasons: 1. The difference was not statistically significant; moreover, statistically significant reductions were not observed among subgroups with greater exposure. 2. The fertility of non-whites with less than 16 years of education increased with exposure, and it would be difficult to conceive of a toxicant which affected only the fertility of whites and college-educated non-whites. 3. Studies recently completed at four other chemical plants (including three where exposure areas could be defined more precisely) lend no support for the notion that occupational exposure to DNT or TDA has reduced male fertility.[7]

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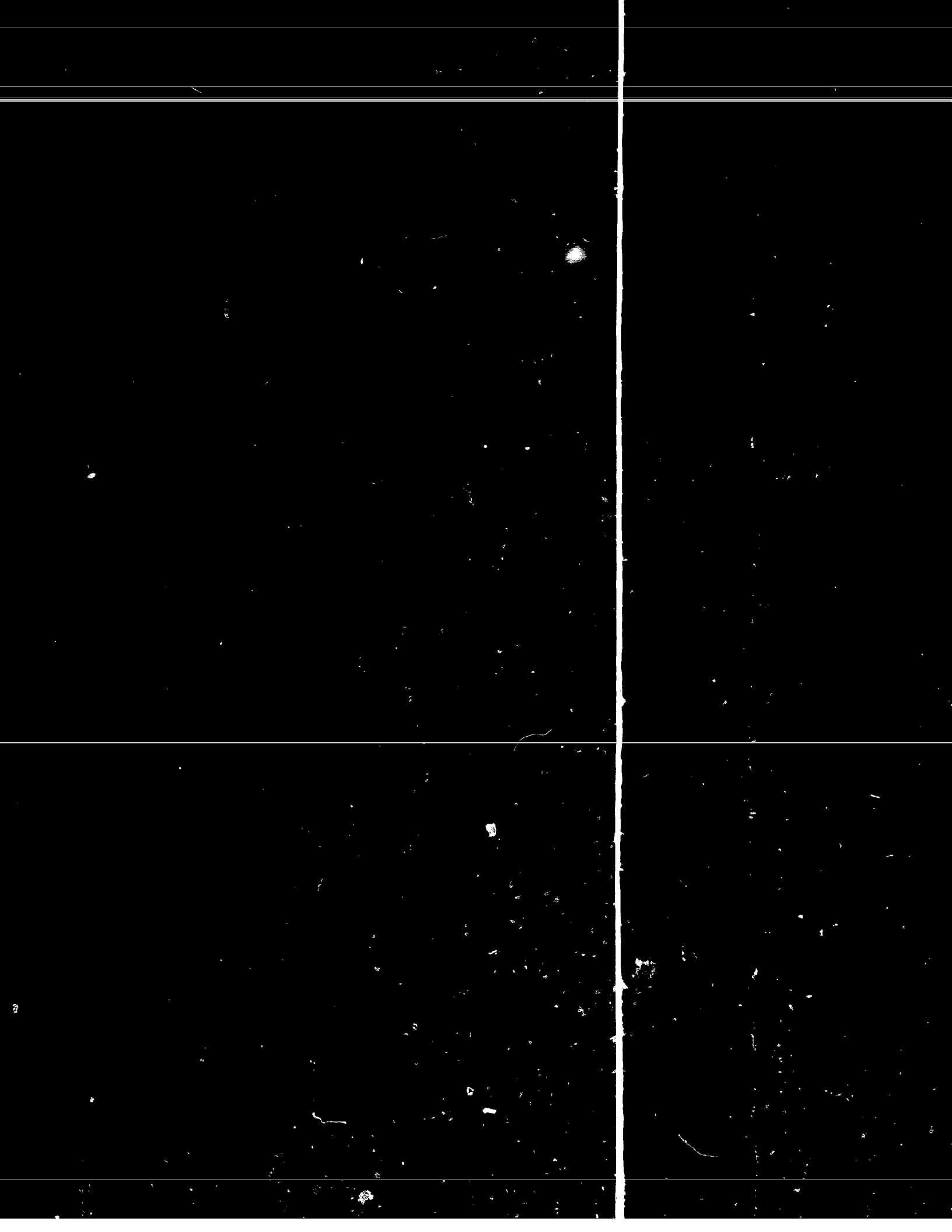

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Group	Pre-Employment O/E	Pre-Employment SFR	TDI O/E	TDI SFR	O/E									
All employees	324/230.0	1.41	46/37.6	1.22	28/21.1	1.33								
All male	303/218.7	1.39	46/37.1	1.24	28/20.9	1.34								
Whites														
≥ 16 yrs school	258/174.9	1.48	38/31.6	1.20	23/19.2	1.20								
< 16 yrs school	26/ 17.7	1.47	8/ 4.7	1.70	0/ 0.0	---								
	232/151.2	1.48	30/26.8	1.12	23/19.2	1.20								
Non-whites														
≥ 16 yrs school	45/ 43.8	1.03	8/ 5.5	1.45	5/ 1.7	2.94								
< 16 yrs school	7/ 4.2	1.67	1/ 1.2	0.83	0/ 0.0	---								
	38/ 39.6	0.96	7/ 4.4	1.59	5/ 1.7	2.94								
All whites & non-whites w ≥ 16 yrs school	265/179.1	1.48	39/32.7	1.19	23/19.2	1.20								
TDI-exposed men	300/217.6	1.38	45/36.8	1.22	28/20.9	1.34								
All whites & non-whites w ≥ 16 yrs school	262/178.0	1.47	38/32.4	1.17	23/19.2	1.20								
Non-whites w ≥ 16 yrs school	38/ 39.6	0.96	7/ 4.4	1.59	5/ 1.7	2.94								
Glycol-exposed men	97/ 65.7	1.48	8/10.6	0.75	28/20.9	1.34								
All whites & non-whites w ≥ 16 yrs school	89/ 56.1	1.59	8/10.0	0.80	23/19.2	1.20								
Non-whites w ≥ 16 yrs	8/ 9.6	0.83	0/ 0.6	0.00	5/ 1.7	2.94								
All females	21/ 11.3	1.85	0/ 0.5	0.00	0/ 0.2	0.00								

O/E - observed/expected births; SFR - standardized fertility ratio; TDI - includes unloading dinitrotoluene and the manufacture of toluene diamine, ca
hydrogen, phosgene, and toluene diisocyanate; Glycol - the manufacture of (ethylene)1-4 glycols from ethylene oxide and the production of ethylene ox
ethylene and oxygen; Basagran - a soybean herbicide: the following chemicals are included in the process: anthranilic acid, isopropyl sulfonamide, d
SO_2, phosgene; G, Chlorine - chlorine manufacture using the mercury cell process; Multiple - potential for multiple exposures not limited to a singl
area, as with various maintenance, laboratory, and salaried positions; Other - administrative and certain technical jobs with little or no opportuni
layoff or other absences, and experience in the following areas: caustic, brine, polyols, butanediol, methylene bisphenyl isocyanate, utilities, of
rine production areas without potential for mercury exposure.

*Expected births were rounded to the nearest tenth.

Table 2

TDI MANUFACTURING: EXPOSURE INTENSITY BY JOB TITLE

Exposure Intensity			
None	Low	Medium	High
materials control clerk	general utility laborer	lab technician	mechanic
stenographer	maintenance engineering technician	sr. lab technician	maint. mechanic
secretary	planner & scheduler	aux. operator, operator C	chem. maint. mech apprentice
gen. office clerk	instrument technician	relief operator	mech. apprentice
production shipping clerk	sr. instr. technician	detail relief foreman	maint. trainee
sr. process improvement engineer	instr. tech. trainee	shift foreman	asst. operator, operator B
eng. associate	operator, operator A	day foreman	maint. helper
director of manufacturing isocyanates	sr. staff engineer	shift supervisor	
	foreman	chem. engr. II	
	maintenance foreman		
	relief foreman		
	instrument foreman		
	training foreman		
	operations supervisor		
	operations engineer		
	jr. engineer		
	process engineer		
	assistant manager		
	plant manager		
	production manager		
	superintendent, TDI		
	supervisor - instruments		
	engineering assistant		
	superintendent, works engineering		
	isocyanates specialist		
	gen. services operator		

Table 3

TDI-EXPOSED MALES: All Whites & Non-Whites w ≥ 16 Yrs Education

MARRIED FERTILITY BY DURATION AND INTENSITY OF EXPOSURE

Exposure Duration	Exposure Intensity					
	Low		Medium		High	
	O/E	SFR	O/E	SFR	O/E	SFR
≤ 1.5 years	5/5.3	0.95	5/4.0	1.25	14/6.6	2.13
> 1.5 years	7/6.3	1.12	2/5.1	0.39	5/5.2	0.96

Table 4

TDI-EXPOSED MALES: MARRIED FERTILITY BY PARITY AND WORK AREA*

Group	Pre-Employment		Post-Employment											
			Work Area											
			TDI		Glycol		Basagran		G_2 Chlorine		Multiple		Other	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
TDI-exposed males	300/217.6	1.38	45/36.8	1.22	28/20.9	1.34	5/3.7	1.35	5/2.6	1.92	14/9.0	1 56	55/49.5	1.11
All whites & non-whites w ≥ 16 yrs school	262/178.0	1.47	38/32.4	1.17	23/19.2	1.20	4/2.7	1.48	5/2.6	1.92	12/8.4	1.43	47/44.4	1.06
Parity 0	102/ 27.7	3.68	14/ 4.9	2.86	5/ 1.3	3.85	1/0.4	2.50	0/0.0	----	3/0.6	5.00	8/ 2.2	3.64
Parity 1	88/ 83.2	1.06	14/10.9	1.28	6/ 5.7	1.05	2/1.5	1.33	1/0.2	5.00	5/3.3	1.52	20/14.6	1.37
Parity 2	44/ 35.2	1.25	8/ 9.6	0.83	8/ 5.0	1.60	1/0.6	1.67	1/0.9	1.11	1/1.8	0.56	9/12.8	0.70
Parity 3	18/ 20.2	0.89	2/ 3.0	0.67	3/ 3.3	0.91	0/0.1	0.00	0/0.5	0.00	2/1.2	1.67	7/ 8.5	0.82
Parity 4+	10/ 11.8	0.85	0/ 3.9	0.00	1/ 3.8	0.26	0/0.1	0.00	3/1.1	2.73	1/1.4	0.71	3/ 6.5	0.46
Parity 1+	160/150.4	1.06	24/27.4	0.88	18/17.8	1.01	3/2.3	1.30	5/2.7	1.85	9/7.7	1.17	39/42.4	0.92
Non-whites w ≤ 16 yrs school	38/ 39.6	0.96	7/ 4.4	1.59	5/ 1.7	2.94	1/1.0	1.00	0/0.0	----	2/0.6	3.33	8/ 5.1	1.57
Parity 0	7/ 4.1	1.71	1/ 0.8	1.25	1/ 0.4	2.50	0/0.0	----	0/0.0	----	1/0.2	5.00	2/ 1.1	1.82
Parity 1	14/ 13.8	1.01	3/ 1.5	2.00	1/ 0.3	3.33	1/0.1	10.00	0/0.0	----	0/0.1	0.00	2/ 1.3	1.54
Parity 2	6/ 10.7	0.56	2/ 1.5	1.33	2/ 0.4	2.50	0/0.4	0.00	0/0.0	----	1/0.3	3.33	4/ 0.9	4.44
Parity 3	2/ 3.2	0.63	1/ 0.4	2.50	1/ 0.5	2.00	0/0.4	0.00	0/0.0	----	0/0.0	----	0/ 1.8	0.00
Parity 4+	9/ 8.0	1.13	0/ 0.2	0.00	0/ 0.1	0.00	0/0.1	0.00	0/0.0	----	0/0.0	----	0/ 0.0	----
Parity 1+	31/ 35.7	0.87	6/ 3.6	1.67	4/ 1.3	3.08	1/1.0	1.00	0/0.0	----	1/0.4	2.50	6/ 4.0	1.50

O/E - observed/expected births; SFR - standardized fertility ratio; TDI - includes unloading dinitrotoluene and the manufacture of toluene diamine, carbon monoxide, hydrogen, phosgene, and toluene diisocyanate; Glycol - the manufacture of $(ethylene)_{1-4}$ glycols from ethylene oxide and the production of ethylene oxide from ethylene and oxygen; Basagran - a soybean herbicide: the following chemicals are included in the process: anthranilic acid, isopropyl sulfonamide, diisopropyl urea, SO_3, phosgene; G_2 Chlorine - chlorine manufacture using the mercury cell process; Multiple - potential for multiple exposures not limited to a single production area, as with various maintenance, laboratory, and salaried positions; Other - administrative and certain technical jobs with little or no opportunity for exposure, layoff or other absences, and experience in the following areas: caustic, brine, polyols, butanediol, methylene bisphenyl isocyanate, utilities, offsites, and chlorine production areas without potential for mercury exposure.

*Expected births were rounded to the nearest tenth.

Table 5

GLYCOL-EXPOSED MALES: MARRIED FERTILITY BY PARITY AND WORK AREA*

Group	Pre-Employment		Post-Employment Work Area											
			TDI		Glycol		Basagran		G_2 Chlorine		Multiple		Other	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
Glycol-exposed males	97/65.7	1.48	8/10.6	0.75	28/20.9	1.34	3/0.7	4.29	3/1.1	2.73	5/4.6	1.09	37/31.1	1.19
All whites & non-whites w ≥ 16 yrs school	89/56.1	1.59	8/10.0	0.80	23/19.2	1.20	2/0.6	3.33	3/1.1	2.73	5/4.6	1.09	33/27.4	1.20
Parity 0	39/10.4	3.75	1/ 1.4	0.71	5/ 1.3	3.85	0/0.1	0.00	0/0.0	----	1/0.0	----	4/ 0.8	5.00
Parity 1	26/28.4	0.92	4/ 1.6	2.50	6/ 5.7	1.05	1/0.2	5.00	0/0.0	----	1/1.9	1.[illegible]	13/ 9.3	1.40
Parity 2	16/ 9.1	1.76	2/ 3.3	0.61	8/ 5.0	1.60	1/0.1	10.00	0/0.3	0.00	0/0.8	0.[illegible]	6/ 6.5	0.92
Parity 3	5/ 4.7	1.06	1/ 1.2	0.83	3/ 3.3	0.91	0/0.1	0.00	0/0.1	0.00	2/1.0	2.00	7/ 5.7	1.23
Parity 4+	3/ 3.6	0.83	0/ 2.1	0.00	1/ 3.8	0.26	0/0.1	0.00	3/0.8	3.75	1/0.8	1.25	3/ 4.9	0.61
Parity 1+	50/45.8	1.09	7/ 8.2	0.85	18/17.8	1.01	2/0.5	4.00	3/1.2	2.50	4/4.5	0.89	29/26.4	1.10
Non-whites w ≤ 16 yrs scho[illegible]	8/ 9.6	0.83	0/ 0.6	0.00	5/ 1.7	2.94	1/0.1	10.00	0/0.0	----	0/0.0	----	4/ 3.7	1.08
Parity 0	2/ 1.0	2.00	0/ 0.1	0.00	1/ 0.4	2.50	0/0.0	----	0/0.0	----	0/0.0	----	1/ 0.8	1.25
Parity 1	4/ 2.8	1.43	0/ 0.2	0.00	1/ 0.3	3.33	1/0.1	10.00	0/0.0	----	0/0.0	----	1/ 1.2	0.83
Parity 2	2/ 5.0	0.40	0/ 0.1	0.00	2/ 0.4	5.00	0/0.0	----	0/0.0	----	0/0.0	----	2/ 0.3	6.67
Parity 3	0/ 0.8	0.00	0/ 0.2	0.00	1/ 0.5	2.00	0/0.0	----	0/0.0	----	0/0.0	----	0/ 1.4	0.00
Parity 4	0/ 0.0	----	0/ 0.0	----	0/ 0.1	0.00	0/0.0	----	0/0.0	----	0/0.0	----	0/ 0.0	----
Parity 1+	6/ 8.6	0.70	0/ 0.5	0.00	4/ 1.3	3.08	1/0.1	10.00	0/0.0	----	0/0.0	----	3/ 2.9	1.03

O/E - observed/expected births; SFR - standardized fertility ratio; TDI - includes unloading dinitrotoluene and the manufacture of toluene diamine, carbon monoxide, hydrogen, phosgene, and toluene diisocyanate; Glycol - the manufacture of $(ethylene)_{1-4}$ glycols from ethylene oxide and the production of ethylene oxide from ethylene and oxygen; Basagran - a soybean herbicide: the following chemicals are included in the process: anthranilic acid, isopropyl sulfonamide, diisopropyl urea, SO_3, phosgene; G_2 Chlorine - chlorine manufacture using the mercury cell process; Multiple - potential for multiple exposures not limited to a single production area, as with various maintenance, laboratory, and salaried positions; Other - administrative and certain technical jobs with little or no opportunity for exposure, layoff or other absences, and experience in the following areas: caustic, brine, polyols, butanediol, methylene bisphenyl isocyanate, utilities, offsites, and chlorine production areas without potential for mercury exposure.

*Expected births were rounded to the nearest tenth.

Table 6

ABNORMALITIES OR DEFECTS REPORTED IN LIVEBORN OFFSPRING

MALES, MARRIED EXPERIENCE

Group	Number with Abnormalities/Defects	Live Births	Ratio
All males			
Pre-employment	31	306	0.10
Post-employment	10	154	0.06
TDI Exposure	5	46	0.11
Glycol Exposure	1	28	0.04
Basagran Exposure	0	5	0.00
G_2 Chlorine Exposure	0	5	0.00
Multiple Exposure	0	15	0.00
Other Exposure	4	55	0.07

LIST OF ABNORMALITIES AND DEFECTS: MALES

LIVEBORN OFFSPRING OF POST-EMPLOYMENT MARRIED EXPERIENCE

muscle in neck short
*feet turn in
*enlarged lymph node on neck
ulcer, lazy eye
+no control over head and neck muscles
*broken collar bone
*oxygen deficiency-slow learner
*hard of hearing
heart murmur - hole in ventricular side of heart
epilepsy

*child conceived during TDI exposure

+child conceived during glycol exposure

Table 7

MISCARRIAGES, STILLBIRTHS, NEONATAL DEATHS: MALES, MARRIED EXPERIENCE

Group	Miscarriages + Stillbirths by Trimester				Neonatal Deaths	Live Births	Miscarriages + Stillbirths + Neonatal Deaths / Total Pregnancies	
	Unk	1	2	3			Number	Percent
All males								
Pre-employment	5	19	4	4	4	306	36/338	11
Post-employment	0	17	9	0	0	154	26/180	14
TDI exposure	0	2	5	0	0	46	7/ 53	13
Glycol exposure	0	1	0	0	0	28	1/ 29	3
Basagran exposure	0	0	0	0	0	5	0/ 5	0
G_2 chlorine exposure	0	0	0	0	0	5	0/ 5	0
Multiple exposure	0	1	1	0	0	15	2/ 17	12
Other exposure	0	13*	3	0	0	55	16/ 71	23
All males (excluding habitual aborters)								
Pre-employment	5	17	3	4	4	305	33/334	10
Post-employment	0	17	5	0	0	154	22/176	13
TDI exposure	0	2	1	0	0	46	3/ 49	6
Glycol exposure	0	1	0	0	0	28	1/ 29	3
Basagran exposure	0	0	0	0	0	5	0/ 5	0
G_2 chlorine exposure	0	0	0	0	0	5	0/ 5	0
Multiple exposure	0	1	1	0	0	15	2/ 17	12
Other exposure	0	13*	3	0	0	55	16/ 71	23

*Includes one miscarriage conceived less than nine months from the date of interview

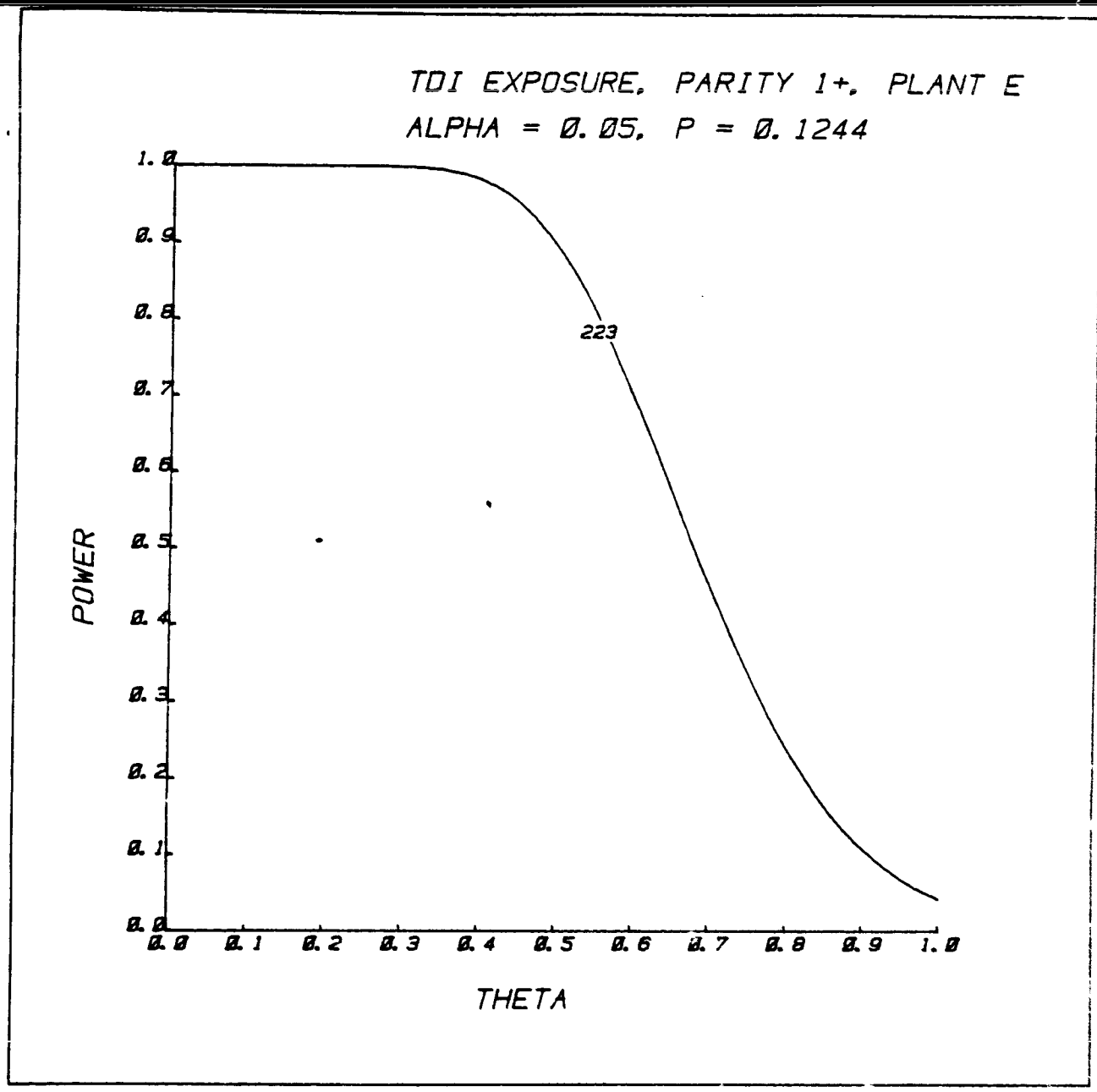

Figure 1 - Power of detecting exposure-related decreases in fertility among the parity 1+ experience of TDI-exposed men with a college education and white men with less than four years of college. N = 223 is the total number of observed births; p = 0.1244 is the proportion of births expected to occur during the period at risk from exposure; alpha = 0.05 is the level of significance (one-sided test); and theta is the proportional change in fertility with exposure.

APPENDIX I: EXPOSURE CODES FOR WHICH INDIVIDUAL FERTILITY ANALYSES ARE AVAILABLE

--P115
JOB EXPOSURE CODES

002	TDI
003	Chlorine, General; Cell Repair, general
004	Chlorine, C_2 (Mercury
005	Chlorine, C_1 or C_3
006	Basagran
007	Caustic, Brine
008	Glycol
009	Polyols
010	At plant--no exposure
011	Butanediol
012	MDI
013	Utilities
014	Organics (mostly EO/EG)
015	Plant-wide Strike
016	Offsites (bugpond, dock, repairing pipes)
017	Electrolytics, general
018	Not used
019	Plant-wide, shift (with TDI possibility), multiple exposure such as Lab (non-TDI), docks shipping, shop
020	Medical leave after TDI
021	TDI--multiple (simultaneous assignment to TDI and other area)
022	Not used
023	Chlorine, general, Cell Repair, general after TDI
024	Chlorine, C_2 (mercury) after TDI
025	Chlorine, C_1 or C_3
026	Basagran after TDI
027	Caustic, Brine after TDI
028	Glycol after TDI
029	Polyols after TDI
030	At plant--no exposure after TDI exposure
031	Butanediol after TDI
032	MDI after TDI
033	Utilities after TDI
034	Organics (mostly EO/EG) after TDI
035	Plant-wide Strike after TDI
036	Offsites after TDI
037	Electrolytics, general after TDI
038	Not used
039	Plant-wide, shift, multiple, etc. after TDI
040	Medical leave after G_2 Chlorine
041	Chlorine G_2-multiple (simultaneous assignment to G_2 Chlorine and other area)
042	TDI after G2 Chlorine
043	Chlorine, general, Cell Repair, general after Chlorine G_2
044	Plant-wide strike after G2 Chlorine
045	Chlorine, G1 or G3 after G2 Chlorine
046	Basagran after G2 Chlorine
047	Caustic, Brine after G2 Chlorine
048	Glycol after G2 Chlorine
049	Polyols after G2 Chlorine
050	At plant-no exposure after G2 Chlorine

(Continued)

--P115

JOB EXPOSURE CODES - Continued

051 Butanediol after G2 Chlorine
052 MDI after G2 Chlorine
053 Utilities after G2 Chlorine
054 Organics (mostly EO/EG) after G2 Chlorine
055 Plant-wide Strike after G2 Chlorine
056 Offsites after G2 Chlorine
057 Electrolytics, general after G2 Chlorine
058 Not used
059 Plant-wide, shift, multiple, etc. after C2 Chlorine
060 Medical leave after Basagran
061 Basagran-multiple (simultaneous exposure to Basagran and another area)
062 TDI after Basagran
063 Chlorine, general, Cell Repair, general after Basagran
064 Chlorine, G2 (mercury) after Basagran
065 Chlorine, G1 or G3 after Basagran
066 Not used
067 Caustic, Brine after Basagran
068 Glycol after Basagran
069 Polyols after Basagran
070 At plant-no exposure after Basagran
071 Butanediol after Basagran
072 MDI after Basagran
073 Utilities after Basagran
074 Organics (mostly EO/EG) after Basagran
075 Plant-wide Strike after Basagran
076 Offsites after Basagran
077 Electrolytics, general after Basagran
078 Not used
079 Plant-wide, shift, multiple, etc. after Basagran
080 Medical Leave after Glycol
081 Glycol-multiple (simultaneous exposure to Glycol and another area)
082 TDI after Glycol
083 Chlorine, general, Cell Repair, general after Glycol
084 Chlorine, G2 (mercury) after Glycol
085 Chlorine, G1 or G3 after Glycol
086 Basagran after Glycol
087 Caustic, Brine after Glycol
088 Not used
089 Polyols after Glycol
090 At plant-no exposure after Glycol
091 Butanediol after Glycol
092 MDI after Glycol
093 Utilities after Glycol
094 Organics (mostly EO/EG) after Glycol
095 Plant-wide Strike after Glycol
096 Offsites after Glycol
097 Electrolytics, general after Glycol
098 Not used
099 Plant-wide, shift, multiple, etc. after Glycol
100 Medical Leave (after other or no exposure)
101 Terminated or transferred from Geismar plant; layoff
201 Terminated or transferred from Geismar plant; layoff after TDI
221 TDI-multiple exposure preceded by TDI
241 G2 Chlorine-multiple exposure preceded by TDI
261 Basagran-multiple exposure preceded by TDI
281 Glycol-multiple exposure preceded by TDI

JOB EXPOSURE CODES

401	Terminated or transferred from Geismar plant; layoff after G2 Chlorine
421	TDI-multiple preceded by G2 Chlorine
441	G2 Chlorine-multiple preceded by G2 Chlorine
461	Basagran-multiple preceded by G2 Chlorine
481	Glycol-multiple preceded by G2 Chlorine
601	Terminated or transferred from Geismar plant; layoff after Basagran
621	TDI-multiple after Basagran
641	G2 Chlorine-multiple after Basagran
661	Basagran-multiple after Basagran
681	Glycol-multiple after Basagran
801	Terminated or transferred from Geismar plant; layoff after Glycol
821	TDI-multiple after Glycol
841	G2 Chlorine-multiple after Glycol
861	Basagran-multiple after Glycol
881	Glycol-multiple after Glycol

X-multiple assigned by order of preference:

TDI > Chlorine (G2) > Basagran > Glycol

APPENDIX II: JOB TITLES FOR WHICH INDIVIDUAL FERTILITY ANALYSES ARE AVAILABLE

P115--

JOB TITLE CODES

Job Title Code	Job Title	Dept.
001	Mechanic I, II, III, 3d cl, maint. mech. (electrician), chem maint mech	Maint.
002	Apprentice I, II, III, IV, mech apprentice, maint trainee	"
003	Gen. Utility (laborer)	"
004	Maint engineering tech	"
005	Clerk	"
006	Planner & scheduler	"
007	Instrument tech trainee	"
008	Instr tech	"
009	Sr. Instr. tech	"
010	Loader & General Helper, Marine Loader	Docks Shipping
011	Lab Tech	Lab
012	Sr. Lab Tech	Lab
013		
014		
015		
016		
017		
018		
019		
020	Brine Operator, Brine Purif. Operator, Caustic operator, water treatment operator	Caustic/Cl2/Cell Rep Elec. Mfg./
021	Loader & gen helper	"
022	Cell repair helper	"
023	Cell repairman	"
024	Cell repair leader	"
025	Cell room operator	"
026	Control room operator	"
027	Liquefaction operator	"
028	Relief operator	"
029	Laborer	"
030	Trainee-caustic	"
031	Trainee--Cell repair	"
032	Loader (chlorine)	"
033	Operator helper	"
034	Maint. helper	"
035	Auxiliary operator (caustic)	"
036	Caustic production clerk, cell room clerk	"
037	Trainee--G1 or G3	"
038	Loader--caustic	"
039		
040	Isocyanates operator, isocyanate operator A	TDI
041	Asst. isocyanate operator, isocyanate operator B	"
042	Auxiliary operator, isocyanate operator C	"
043	Relief Operator	"
044	Materials Control Clerk	"
045	Stenographer	"
046	Secretary	"

(Continued)

Job Title Code	Job Title	Dept.
047	General office clerk, temporary clerk	TDI
048	Production shipping clerk	"
049	Detail Relief Foreman	"
050	Glycol Operator (A)	Glycol/Oxy-Glycol
051	Glycol Operator B, asst glycol operator	EO-EG
052	Auxiliary operator (C), aux. glycol operator	"
053	Relief glycol operator, relief operator	"
054	Operator-helper	"
055	Loader & general helper	"
056	Loader	"
057	Glycol compounder (glycol only--antifreeze)	"
058	Shift Foreman	"
059	Glycol Operator	"
060	Operator A	Basagran
061	Operator B	"
062	Relief operator	"
063	Loader	"
064		
065		
066	Operator B, Assistant Operator, Asst. Butanediol	Butanediol
067	Relief Operator	"
068	Trainee	"
069	Loader	"
070	Operator (A)	MDI
071	Asst. Operator (B), Operator B	"
072	Operator C	"
073	Relief Operator	"
074	Maint. Mech.	"
075	Production Clerk	"
076	Superintendent	"
077	Tech. Mgr.	"
078		
079		
080	Polyols Operator	Polyol
081	Operator C	"
082	Relief Operator	"
083	Operator A	Utilities
084	Operator B, Aux. Operator, Asst. Op., Asst. Util. Op.	"
085	Operator C	"
086	Relief Operator	"
087	Boiler Operator	"
088	Water Treatment Operator	"
089	Treatment plant operator	"
090	Waste treatment operator	"
091	Trainee	"
092	Clerk	General Stores
093	Stenographer	Administrative
094	Secretary	"
095	Accounting Clerk	"
096	Sr. Staff Eng.	TDI
097		
098	Not at plant (terminated, strike, la offs)	No exposure
~~099~~	~~Medical leave (This code deleted)~~	~~No exposure~~

Job Title Code	Job Title	Dept.
100		
101	Foreman, Maint. Foreman, Relief Foreman	Maint.
102	Instr. Foreman	"
103	Shift Foreman	Elec. Mfg./Caustic/ Cl_2/Cell Repair
104	Temporary Foreman	"
105	Operations Supervisor	TDI
106	Shift Foreman	"
107	Day Foreman (TDI/Polyol)	"
108	Training Foreman	"
109	Shift Supervisor	"
110	Operations Technical Supervisor, Operations Supv.	"
111	Operations Engineer	"
112	Jr. Engineer	"
113	Process Engineer	"
114	Sr. Process Improvement Engr.	"
115	Eng. Associate	"
116	Asst. Mgr.	"
117	Plant Mgr., Mgr.	"
118	Director of Mfg. Isocyanates (TDI, MDI, Polyol)	"
119	Production Manager	"
120	Superintendent	"
121	Shift Foreman	Basagran
122	Tank Farm Day Supervisor	"
123	Shift Supervisor	"
124	Shift Foreman	Butanediol
125	Shift Foreman	Polyol
126	Tech. Supvr., Superintendent	"
127	Process Engineer	Utilities
128	Shift Supervisor	Services
129	Jr. Engineer	Works Eng'g
130	Tech. Supervisor	"
131	Supervisor--Instruments	"
132	Operations Supervisor	"
133	Superintendent	"
134	Maint. Foreman	"
135	Eng. Assistant	Process Eng'g
136	Process Engineer	"
137	Shift Foreman	Utilities
138	Isocyanates Specialist	TDI
139	Chem Eng II	Works Eng'g
140		
141		
142		
143		
144		
145		
146		
147		
148		
149		
150	Maint. Helper	Works Eng'g
151	General Services Operator	"
152	"A" Operator	Butanediol
153	Trainee-Glycol	Glycol/Oxy-Glycol/ EO-EG

APPENDIX III: AN EXAMPLE OF A CODED QUESTIONNAIRE

Male Employee

Employee No. 0000002

For Office Use

RACE: White 1 Non-White 2 — 1

1. Are you presently married, widowed, divorced, separated, or have you never been married?

Married 1 Widowed 2 Divorced 3 Separated 4 Never Married 5 — 1

If never married: Skip to Q22

2. *If presently married and not separated:*

Is your wife currently employed full-time? Yes 1 No 2 — 2

3. How many times have you been married? 1 — 1

Now I would like to ask you some questions about your (present/last/ex-) wife:

4. When was she born?

10 (Mo) 17 (Day) ~~81~~ 50 (Year) — 10 17 50

5. When were you and she married?

10 (Mo) 14 (Day) 72 (Year) — 10 14 72

If presently married and not separated: Skip to Q7

6. When did you become widowed/permanently separated from her?

__ (Mo) __ (Day) __ (Year) — 88 88 88

7. How many times has your (present/last/ex-) wife been married? 1 — 1

1: *Skip to Q12.*

2+: *Go to Q8.*

8. When was she first married?

__ (Mo) __ (Year) — 88 88

9. When did she become widowed or permanently separated from her first husband?

__ (Mo) __ (Year) — 88 88

If married only twice: Skip to Q12.

10. When was she married for the second time?

__ (Mo) __ (Year) — -- --

For Office Use

11. When did she become widowed or permanently separated from her second husband?

__ Mo __ __ Year — — — —

12. How many babies has your (present/last/ex-) wife ever had, not counting miscarriages, stillbirths, stepchildren or adopted children?

2 No. 02

If none: Skip to Q17

13. Now I would like to know the birth dates and sex of all her children, beginning with the oldest. (*Ask about as many children as were indicated in Q12*).

•Was the first child a boy or a girl? Male 1 Female 2 ~~Female 2~~ 2

When was he/she born? 0 8 Mo 1 3 Day 7 6 Year 08 13 76

•Was the second child a boy or a girl? Male 1 Female 2 ~~Female 2~~ 2

When was he/she born? 0 3 Mo 2 0 Day 8 0 Year 03 20 80

•Was the third child a boy or a girl? Male 1 Female 2 —

When was he/she born? __ Mo __ Day __ Year — — — — — —

•Was the fourth child a boy or a girl? Male 1 Female 2 —

When was he/she born? __ Mo __ Day __ Year — — — — — —

•Was the fifth child a boy or a girl? Male 1 Female 2 —

When was he/she born? __ Mo __ Day __ Year — — — — — —

•Was the sixth child a boy or a girl? Male 1 Female 2 —

When was he/she born? __ Mo __ Day __ Year — — — — — —

•Was the seventh child a boy or a girl? Male 1 Female 2 —

When was he/she born? __ Mo __ Day __ Year — — — — — —

•Was the eighth child a boy or a girl? Male 1 Female 2 —

When was he/she born? __ Mo __ Day __ Year — — — — — —

If more than eight children, continue on Family History Questionnaire Supplement.

Employee No. 0000002

For Office Use

14. At birth, did any of your (present/last/ex-) wife's children remain in the hospital after she had gone home?

(Yes 1) No 2 → 1

If yes:

How many of your (present/last/ex-) wife's children remained in the hospital after she had gone home? 1 → 1

Was the first child a boy or girl? Male 1 (Female 2) → 2

When was he/she born? Mo 8 Day 13 Year 76 → 08 13 76

Reason for longer hospital stay: yellow jaundice 1-2 days in hosp → –

Was the second child a boy or girl? Male 1 Female 2 → –

When was he/she born? Mo __ Day __ Year __ → – – – – – –

Reason for longer hospital stay: _____ → –

Was the third child a boy or girl? Male 1 Female 2 → –

When was he/she born? Mo __ Day __ Year __ → – – – – – –

Reason for longer hospital stay: _____ → –

For Office Use

15. Did any of your (present/last/ex-) wife's children have an abnormality or defect?

Yes 1 No 2 — 2

If yes:

How many children were involved? _____ --

Was the (first) child a boy or a girl? Male 1 Female 2 —

When was he/she born? ___ ___ ___ ___ ___ ___ — — — — — —
Mo Day Year

What was the abnormality or defect? _____

_____

_____

Was the second child a boy or a girl? Male 1 Female 2 —

When was he/she born? ___ ___ ___ ___ ___ ___ — — — — — —
Mo Day Year

What was the abnormality or defect? _____

_____

_____

Was the third child a boy or a girl? Male 1 Female 2 —

When was he/she born? ___ ___ ___ ___ ___ ___ — — — — — —
Mo Day Year

What was the abnormality or defect? _____

_____

_____

Was the fourth child a boy or a girl? Male 1 Female 2 —

When was he/she born? ___ ___ ___ ___ ___ ___ — — — — — —
Mo Day Year

What was the abnormality or defect? _____

_____

_____

If more than four children, continue on Family History Questionaire Supplement

Employee No. 0000001

For Office Use

16. Are all of your (present/last/ex-) wife's children living?

(Yes) 1 No 2 — 1

If no:

How many children have died? _____ —

•Was the (first) child a boy or a girl? Male 1 Female 2 —

When was he/she born? ___ Mo ___ Day ___ Year — — — — — —

When did he/she die? ___ Mo ___ Day ___ Year — — — — — —

What was the cause of his/her death? _____

_____

_____ — —

•Was the second child a boy or a girl? Male 1 Female 2 —

When was he/she born? ___ Mo ___ Day ___ Year — — — — — —

When did he/she die? ___ Mo ___ Day ___ Year — — — — — —

What was the cause of his/her death? _____

_____

_____ — —

•Was the third child a boy or a girl? Male Female 2 —

When was he/she born? ___ Mo ___ Day ___ Year — — — — — —

When did he/she die? ___ Mo ___ Day ___ Year — — — — — —

What was the cause of his/her death? _____

_____

_____ — —

For Office Use

Was the fourth child a boy or a girl? Male 1 Female 2 —

When was he/she born? ___ Mo ___ Day ___ Year — — — — — —

When did he/she die? ___ Mo ___ Day ___ Year — — — — — —

What was the cause of his/her death? _____

_____ —

_____ —

If more than four children, continue on Family History Questionnaire Supplement.

17. Has your (present/last/ex-) wife ever had a miscarriage or a stillborn child?

Yes 1 No 2 1

If yes:

How many times did she miscarry or deliver a stillborn child? 1 1

When was the first? ___ Mo ___ Day 7 9 Year — — — — 7 9

How many months pregnant was she at the time? 2-3 2.5

When was the second? ___ Mo ___ Day ___ Year — — — — — —

How many months pregnant was she at the time? _____ —

When was the third? ___ Mo ___ Day ___ Year — — — — — —

How many months pregnant was she at the time? _____ —

When was the fourth? ___ Mo ___ Day ___ Year — — — — — —

How many months pregnant was she at the time? _____ —

When was the fifth? ___ Mo ___ Day ___ Year — — — — — —

How many months pregnant was she at the time? _____ —

When was the sixth? ___ Mo ___ Day ___ Year — — — — — —

How many months pregnant was she at the time? _____ —

If more than six miscarriages/stillbirths continue on Family History Questionnaire Supplement.

Employee No. 0 0 0 0 0 0 1

For Office Use

18. Has your (present/last/ex-) wife ever had a pregnancy terminated by medical or surgical means which did not result in a live birth?

Yes 1 (No 2) — 2

If yes:

How many such pregnancies has she had terminated by medical or surgical means? _____ — —

When was the first?
Mo ___ Day ___ Year ___ — — — — — —

How many months pregnant was she at the time? _____ —

When was the second?
Mo ___ Day ___ Year ___ — — — — — —

How many months pregnant was she at the time? _____ —

When was the third?
Mo ___ Day ___ Year ___ — — — — — —

How many months pregnant was she at the time? _____ —

When was the fourth?
Mo ___ Day ___ Year ___ — — — — — —

How many months pregnant was she at the time? _____ —

When was the fifth?
Mo ___ Day ___ Year ___ — — — — — —

How many months pregnant was she at the time? _____ —

When was the sixth?
Mo ___ Day ___ Year ___ — — — — — —

How many months pregnant was she at the time? _____ —

19. Has there ever been a time when you and your (present/last/ex-) wife did not use contraception for at least a year and a pregnancy did not result?

Yes 1 (No) 2 — 2

If yes:

When?
Mo ___ Year ___ to Mo ___ Year ___ — — — — — — — —

Mo ___ Year ___ to Mo ___ Year ___ — — — — — — — —

Mo ___ Year ___ to Mo ___ Year ___ — — — — — — — —

For Office Use

20. Has your (present/last/ex-...) wife had any operation, such as a hysterectomy, or tubal ligation, which made her unable to have children?

If yes: (Yes) 1 No 2 — 1

Which operations were performed and when?

Hysterectomy 2 — ___ Mo ___ Year — — — — —

Tubal Ligation 3 — ___ Mo ___ Year — — — — —

_____ Other — ___ Mo ___ Year — — — — —
Nature of Operation

21. Has your (present/last/ex-...) wife ever had a D&C (scraping of the lining of the womb) or any other female operation not listed above? Yes ___ No ✓ — 2

If yes:

Which operations were performed and when?

1 D&C — ___ Month ___ Year — — — — —

1 D&C — ___ Month ___ Year — — — — —

1 D&C — ___ Month ___ Year — — — — —

_____ Other — ___ Month ___ Year — — — — —
(Describe)

_____ Other — ___ Month ___ Year — — — — —
(Describe)

22. What is the highest grade of school you completed? 1 4 — 14

Elem: 01-08 H.S.: 09-12 College: 13-16 Grad: 17-
(Interview ends for never married persons)

23. What is the highest grade of school your (present/last/ex-...) wife completed? 1 2 — 12

Elem: 01-08 H.S.: 09-12 College: 13-16 Grad: 17-
(Interview ends for persons married once/twice)

APPENDIX II

LIST OF JOb TITLES FOR WHICH INDIVIDUAL FERTILITY ANALYSES ARE AVAILABLE

Olin Lake Charles

	Job Title Code	Job Title Description
*	001	Accountant/Cost Accountant
	002	Boilermakers/Pipefitters
	003	Bus Driver
*	004	Buyer/Sr. Buyer/Purchasing Agent
	005	Carpenters
	006	Chemist/Shift Chemist
	007	Chemist, Sr. Dev.
*	008	Clerks/Mail Clerk/Payroll/Storekeeper
*	009	Degree Engineers/Sr. Asso. Mech. Eng./Process
*	010	Engineer, Maintenance
*	011	Engineer, Project
*	012	Engineer, Safety
*	013	Expeditor
*	014	Foreman
*	015	Foreman, Maintenance
	016	Helper/General Helper
*	017	Industrial Hygienist/Sr. Ind. Hyg.
	018	Instrument Man/Electrician (I & E)
	019	Insulators/Insulator Trainee
	020	Janitor
	021	Laborers
	023	Lab Tech/Lab Analyst
	024	Machinist
	025	Maintenance Coordinator
	026	Mechanics
	027	Millwrights/Millwrights (training)
	028	Oilers/Painters
	029	Operator/Operator (relief)/Operator Trainee/Lead Operator
*	030	Packout-Loading
*	031	Process Control Specialist
*	032	Production Manager/Superintendent
*	033	Registered Nurse
*	034	Safety Tech/First Aid Man/Loss Prevention Tech/Lead Safety Tech
*	035	Supervisor (Specific Area)
*	036	Supervisor, Engineering
*	037	Supervisor, I & E
*	038	Supervisor, I & E Field
*	039	Supervisor, Sr. Accounting
	040	Superintendent/General supertendent/Superintendent Planning & Scheduling
	041	Truck Driver/Heavy Equipment
*	042	Welders
*	043	Work Coordinator (shift)
*	044	Zone Controller
*	045	Pilot (floating student)
*	046	Foreman, Lab/Temporary
*	047	Manager, Safety/Mgr., Safety & Loss Prevention
*	048	Supervisor, Maintenance
*	049	Superintendent, Maintenance
*	050	Services & Euipment Coordinator
*	051	Supervisor, Safety
*	052	Planner
	053	Process Tech
	054	Finishing Operator/Relief Foreman
	055	Superintendent - Hydrazine Operations Manager
	099	Medical leave or not at plant after working at plant

* [illegible]

APPENDIX III

FERTILITY AND OCCUPATIONAL HISTORY PORTIONS OF THE QUESTIONNAIRE AND RELATED CODE SHEETS

Employee No. #5

For Office

Card 4/6

Race: White (1) Black 2 Other 3 (American Indian, Asian or Pacific Islander, etc.) / (7)

1. Are you presently married, widowed, divorced, separated, or have you never been married?

   Married (1) Widowed 2 Divorced 3 Separated 4 Never Married 5 / (8)

   If never married: Skip to Q13.

2. *If presently married and not separated:*

   Is your wife currently employed? Yes 1 No (2) 2 (9)

3. How many times have you been married? once / (10)

4. In what month and year was your (present/last/ex-) wife born? (11-14)

   04 / 49
   Mo / Year

5. In what month and year were you and your (present/last/ex-) wife married? (15-18)

   11 / 71
   Mo / Year

   If presently married and not separated: Skip to Q7.

6. In what month and year did you become widowed/permanently separated from your (present/last/ex-) wife? (19-22)

   Mo / Year

7. Was this your (present/last/ex-) wife's first marriage? 2 (23)

   Yes 1 *Skip to Q10.*

   No (2) *Go to Q8.*

8. In what year was your (present/last/ex-) wife first married? 70 (24-25)

   70
   Year

9. In what year did your (present/last/ex-) wife become widowed or permanently separated from her first husband? 80 (26-27)

10. How many babies has your (present/last/ex-) wife ever had, not counting miscarriages or stillbirths? Include all children ever born to her *(from all of her marriages)*, but not stepchildren or adopted children. 2 (28-29)

    No.

#5

For Office Use

•Was the first child a boy or a girl? Male (1) Female 2 — 1 (30)

In what month and year was he/she born? SEP (Mo) 73 (Year) — 0973 (31-34)

•Was the second child a boy or a girl? Male 1 Female (2) — 2 (35)

In what month and year was he/she born? JAN (Mo) 76 (Year) — 0176 (36-39)

•Was the third child a boy or a girl? Male 1 Female 2 — (40)

In what month and year was he/she born? ___ (Mo) ___ (Year) — (41-44)

•Was the fourth child a boy or a girl? Male 1 Female 2 — (45)

In what month and year was he/she born? ___ (Mo) ___ (Year) — (46-49)

•Was the fifth child a boy or a girl? Male 1 Female 2 — (50)

In what month and year was he/she born? ___ (Mo) ___ (Year) — (51-54)

•Was the sixth child a boy or a girl? Male 1 Female 2 — (55)

In what month and year was he/she born? ___ (Mo) ___ (Year) — (56-59)

•Was the seventh child a boy or a girl? Male 1 Female 2 — (60)

In what month and year was he/she born? ___ (Mo) ___ (Year) — (61-64)

•Was the eighth child a boy or a girl? Male 1 Female 2 — (65)

In what month and year was he/she born? ___ (Mo) ___ (Year) — (66-69)

If more than eight children, continue on Family History Questionnaire Supplement.

12. *If presently married and not separated:*

Looking ahead, do you want to have any (more) children?

Yes 1 No (2) Uncertain 3 — 2 (37)

13. What is the highest grade of school you completed? 12 — 12 (38-39)
Elem: 01-08 H.S.: 09-12 College: 13-16 Grad: 17-
(Interview ends for never married persons)

14. What is the highest grade of school your (present/last/ex-) wife completed? 12 — 12 (40-41)
Elem: 01-08 H.S.: 09-12 College: 13-16 Grad: 17-
(Interview ends for ever married persons)

R QUESTIONNAIRE

ID #5

257

p code 70663

4. Age last birthday 33 2APR47

5. Race: [X] White (1) [ ] Black (2) [ ] Other (3)

JOB HISTORY

6. Current work location:

- [•] TDA (1)
- [X] TDI (2)
- [ ] Hydrazine (3)
- [ ] Ketazine (4)
- [ ] R-230 (5)
- [ ] T-101 (6)
- [ ] Ammonia (7)
- [ ] PACE (8)
- [ ] Nitric Acid (9)
- [ ] Nitrate (10)
- [ ] Urea (11)
- [ ] Administration (12)
- [ ] Utilities (13)

Maintenance

- [ ] West (14)
- [ ] Central (15)
- [ ] East (16)
- [ ] Hydrazine, Ketazine (17)
- [X] TDI-TDA (18)
- [ ] PACE (19)
- [ ] Other (20) Specify_____
- [ ] Other (21) Specify_____

7. Current job title or craft:

- [ ] Operator (1)
- [ ] Pack out - loading (2)
- [ ] Foreman (3)
- [ ] Supervisor (4)
- [ ] Clerk (5)
- [ ] Machinist (6)
- [ ] Mechanics (7)
- [ ] Carpenters (8)
- [ ] Oilers and painters (9)
- [ ] Insulator (10)
- [ ] Laborers (11)
- [ ] Janitors (12)
- [ ] Truck driver and Heavy Equipment (13)
- [ ] Boilermakers and pipefitters (14)
- [ ] Welders (15)
- [X] Millwright (16)
- [ ] Engineers (17)
- [ ] I & E (18)
- [ ] Other (19)

8. How long with present job? years 2 months 6
Starting date JUN78

9. How long have you worked at Olin? years 9 months
Starting date: JAN72

10. List previous jobs held at Olin. (Start with the present and work back in time)

1. Location: (see list question 6) TDI - TDA

   Job title or craft (see list question 7) millwright

   Length of time in job: years 2 months 6

   How long ago? (years) JUN 78

2. Location: (see list question 6) T-101

   Job title or craft (see lest question 7) Op.

   Length of time in job: years 2 months 6

   How long ago? (years) JAN 76 - JUN 78

3. Location: (see list question 6) TDI

   Job title or craft (see list question 7) maint. trainee

   Length of time in job: years 1 months 6

   How long ago? (years) 74 - 75

4. Location: (see list question 6) nitrate/fused

   Job title or craft (see list question 7) labor

   Length of time in job: years 2 months

   How long ago (years)? 72 - 74

11. In the past 6 months have you worked for more than 3-4 days in and around TDA or DNT? ☑ Yes (1) ☐ No (2)

12. Do you think you have had any exposure to TDA or DNT? ☑ Yes ☐ No
    If yes, specify 6 times

CCUPATIONAL EXPOSURE

ID:

13. Have you ever worked with any of the following:
    a. weed killers: ☐ yes (1) ☒ No (2) ☐ Don't know (3)

    If yes, list substance(s) and dates work began and ended.

Substance	Began	Ended	Substance	Began	Ended

RJR

* Male Employee *

FAMILY HISTORY QUESTIONNAIRE

For Office Use

Employee No. 00022025 — 00022025

Name: _____ (Last) _____ (First) _____ (Second & Third)

Spanish Surname Yes 1 No 2 —

Plant Location Elmira — 1 C. 120

Sex (Male 1) Female 2 1

Birth Date 04 (Mo) 02 (Day) 47 (Yr) 040247

Current Address _____ (Street and Number)

_____ (Town) 14663 (Zip) 14663

Telephone: (____) _____ - _____

Date of Interview 01 (Mo) 29 (Day) 81 (Yr) 012981

Interviewer _____ 2

WORK HISTORY

	Date of Change (Mo / Day / Year)	Department	Job Title	Exposure	For Office Use WKMO	WKDA	WKYR	TTL	EX
1.	01 / __ / 73	Nitrate	Laborer		01	__	73	021	01
2.	01 / __ / 73	Urea	Laborer		01	__	73	021	01
3.	01 / __ / 74	TDI - TDI	Maintenance Millwright (Training)		01	__	74	026	00
4.	01 / __ / 76	T-101	Operator		01	__	76	028	00 → 04
5.	06 / __ / 78	Mnty. TDI-TDM	Millwright		06	__	78	026	00
6.	__ / __ / __				__	__	__	__	__
7.	__ / __ / __				__	__	__	__	__
8.	__ / __ / __				__	__	__	__	__
9.	__ / __ / __				__	__	__	__	__
10.	__ / __ / __				__	__	__	__	__
11.	__ / __ / __				__	__	__	__	__
12.	__ / __ / __				__	__	__	__	__
13.	__ / __ / __				__	__	__	__	__
14.	__ / __ / __				__	__	__	__	__
15.	__ / __ / __				__	__	__	__	__

Male Employee

Employee No. 0 0 2 - 0 5

For Office Use

RACE: (White 1) Non-White 2 — 1

1. Are you presently married, widowed, divorced, separated, or have you never been married?

(Married 1) Widowed 2 Divorced 3 Separated 4 Never Married 5 — 1

If never married: Skip to Q20

2. *If presently married and not separated:*

Is your wife currently employed full-time? Yes 1 (No 2) — 2

3. How many times have you been married? 1 — 1

Now I would like to ask you some questions about your (present/last/ex-) wife:

4. When was she born?

0 3 Mo ___ Day 4 9 Year — 03 -- 49

5. When were you and she married?

0 7 Mo ___ Day 7 1 Year — 07 -- 71

If presently married and not separated: Skip to Q7

6. When did you become widowed/permanently separated from her?

___ Mo ___ Day ___ Year — 88 88 88

7. How many times has your (present/last/ex-) wife been married? 2 (not first time) — 2

1: *Skip to Q12.*

2+: *Go to Q8.*

8. When was she first married?

0 3 Mo 7 0 Year — 03 70

9. When did she become widowed or permanently separated from her first husband?

0 7 Mo 7 0 Year — 07 70

If married only twice: Skip to Q12.

10. When was she married for the second time?

___ Mo ___ Year — -- --

For Office Use

11. When did she become widowed or permanently separated from her second husband?

Mo ___ Year ___ -- --

12. How many babies has your (present/last/ex-) wife ever had, not counting miscarriages, stillbirths, stepchildren or adopted children?

02 No. 02

If none: Skip to Q16

13. Now I would like to know the birth dates and sex of all her children, beginning with the oldest. (*Ask about as many children as were indicated in Q12*).

•Was the first child a boy or a girl? Male 1 (circled) / Female 2 — 1

When was he/she born? 07 Mo ___ Day 73 Year — 07 -- 73

•Was the second child a boy or a girl? Male 1 / Female 2 (circled) — 2

When was he/she born? 01 Mo ___ Day 76 Year — 01 -- 76

•Was the third child a boy or a girl? Male 1 / Female 2 — -

When was he/she born? ___ Mo ___ Day ___ Year — -- -- --

•Was the fourth child a boy or a girl? Male 1 / Female 2 — -

When was he/she born? ___ Mo ___ Day ___ Year — -- -- --

•Was the fifth child a boy or a girl? Male 1 / Female 2 — -

When was he/she born? ___ Mo ___ Day ___ Year — -- -- --

•Was the sixth child a boy or a girl? Male 1 / Female 2 — -

When was he/she born? ___ Mo ___ Day ___ Year — -- -- --

•Was the seventh child a boy or a girl? Male 1 / Female 2 — -

When was he/she born? ___ Mo ___ Day ___ Year — -- -- --

•Was the eighth child a boy or a girl? Male 1 / Female 2 — -

When was he/she born? ___ Mo ___ Day ___ Year — -- -- --

If more than eight children, continue on Family History Questionnaire Supplement.

Employee No. _ _ _ _ _ _ _

For Office Use

14. Did any of your (present/last/ex-) wife's children have an abnormality or defect?

Yes 1 No 2 —

If yes:

How many children were involved? _____ —

Was the (first) child a boy or a girl? Male 1 Female 2 —

When was he/she born? ___ ___ ___ (Mo Day Year) — — — — — —

What was the abnormality or defect? _____

_____

_____ — —

Was the second child a boy or a girl? Male 1 Female 2 —

When was he/she born? ___ ___ ___ (Mo Day Year) — — — — — —

What was the abnormality or defect? _____

_____

_____ — —

Was the third child a boy or a girl? Male 1 Female 2 —

When was he/she born? ___ ___ ___ (Mo Day Year) — — — — — —

What was the abnormality or defect? _____

_____

_____ — —

Was the fourth child a boy or a girl? Male 1 Female 2 —

When was he/she born? ___ ___ ___ (Mo Day Year) — — — — — —

What was the abnormality or defect? _____

_____

_____ — —

If more than four children, continue on Family History Questionaire Supplement

For Office Use

15. Are all of your (present/last/ex-) wife's children living?

Yes 1 No 2 --

If no:

How many children have died? _____ --

•Was the (first) child a boy or a girl? Male 1
Female 2 --

When was he/she born? ___ ___ ___ -- -- -- --
Mo Day Year

When did he/she die? ___ ___ ___ -- -- -- --
Mo Day Year

What was the cause of his/her death? _____

_____

_____ --

•Was the second child a boy or a girl? Male 1
Female 2 --

When was he/she born? ___ ___ ___ -- -- -- --
Mo Day Year

When did he/she die? ___ ___ ___ -- -- -- --
Mo Day Year

What was the cause of his/her death? _____

_____

_____ --

•Was the third child a boy or a girl? Male 1
Female 2 --

When was he/she born? ___ ___ ___ -- -- -- --
Mo Day Year

When did he/she die? ___ ___ ___ -- -- -- --
Mo Day Year

What was the cause of his/her death? _____

_____

_____ --

Employee No. _ _ _ _ _ _ _ _ _

For Office Use

'Was the fourth child a boy or a girl? Male 1 Female 2 _

When was he/she born? ___ ___ ___ (Mo Day Year) __ __ __ __ __ __

When did he/she die? ___ ___ ___ (Mo Day Year) __ __ __ __ __ __

What was the cause of his/her death? _____

_____ __

If more than four children, continue on Family History Questionnaire Supplement.

16. Has your (present/last/ex-) wife ever had a miscarriage or a stillborn child?

Yes 1 No 2 _

If yes:

How many times did she miscarry or deliver a stillborn child? _____ _

'When was the first? ___ ___ ___ (Mo Day Year) __ __ __ __ __ __

How many months pregnant was she at the time? _____ _

'When was the second? ___ ___ ___ (Mo Day Year) __ __ __ __ __ __

How many months pregnant was she at the time? _____ _

'When was the third? ___ ___ ___ (Mo Day Year) __ __ __ __ __ __

How many months pregnant was she at the time? _____ _

'When was the fourth? ___ ___ ___ (Mo Day Year) __ __ __ __ __ __

How many months pregnant was she at the time? _____ _

'When was the fifth? ___ ___ ___ (Mo Day Year) __ __ __ __ __ __

How many months pregnant was she at the time? _____ _

'When was the sixth? ___ ___ ___ (Mo Day Year) __ __ __ __ __ __

How many months pregnant was she at the time? _____ _

If more than six miscarriages/stillbirths continue on Family History Questionnaire Supplement.

For Office Use

17. Has your (present/last/ex-) wife ever had a pregnancy terminated by medical or surgical means which did not result in a live birth?

Yes 1 No 2 _

If yes:

How many such pregnancies has she had terminated by medical or surgical means? _____ __

·When was the first? ___Mo ___Day ___Year __ __ __ __

How many months pregnant was she at the time? _____ _

·When was the second? ___Mo ___Day ___Year __ __ __ __

How many months pregnant was she at the time? _____ _

·When was the third? ___Mo ___Day ___Year __ __ __ __

How many months pregnant was she at the time? _____ _

·When was the fourth? ___Mo ___Day ___Year __ __ __ __

How many months pregnant was she at the time? _____ _

·When was the fifth? ___Mo ___Day ___Year __ __ __ __

How many months pregnant was she at the time? _____ _

·When was the sixth? ___Mo ___Day ___Year __ __ __ __

How many months pregnant was she at the time? _____ _

18. Has there ever been a time when you and your (present/last/ex-) wife did not use contraception for at least a year and a pregnancy did not result?

Yes 1 No 2 _

If yes:

When? ___Mo ___Year to ___Mo ___Year __ __ __ __

___Mo ___Year to ___Mo ___Year __ __ __ __

___Mo ___Year to ___Mo ___Year __ __ __ __

Employee No. 00 _ _ _ _ _

For Office Use

19. Have you or your (present/last/ex-) wife had any operation, such as a vasectomy, hysterectomy, or tubal ligation, which made you unable to have children?

Yes 1 No 2

If yes:

Which operations were performed and when?

		Mo	Year	
Vasectomy	1	___	___	— — — —
Hysterectomy	2	___	___	— — — —
Tubal Ligation	3	___	___	— — — —
_____ Nature of Operation	Other 4	___	___	— — — —

20. What is the highest grade of school you completed? 12 L2
Elem: 01-08 H.S.: 09-12 College: 13-16 Grad: 17-
(Interview ends for never married persons)

21. What is the highest grade of school your (present/last/ex-) wife completed? 12 L2
Elem: 01-08 H.S.: 09-12 College: 13-16 Grad: 17-
(Interview ends for persons married once)

THE REPRODUCTIVE EXPERIENCE OF WORKERS EXPOSED TO DINITROTOLUENE AND TOLUENE DIAMINE AT RUBICON CHEMICALS INCORPORATED, GEISMAR, LOUISIANA

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SUMMARY

An analysis of reproductive experience at Rubicon Chemicals Incorporated's Geismar, Louisiana plant has revealed no evidence for a decrease in fertility related to working in the nitrations or reductions area, where exposures to dinitrotoluene and toluene diamine may occur. Moreover, there was no evidence in these areas of an abnormal aggregation of miscarriages, stillbirths, neonatal deaths, or birth defects.

Exposure to dinitrotoluene and toluene diamine in the workplace has been suspected to impair spermatogenesis and to increase the risk that workers' wives may undergo spontaneous abortion.[1] Since dinitrotoluene and toluene diamine are produced at their plant in Geismar, Louisiana, the management of Rubicon Chemicals Inc. requested CIIT to evaluate the reproductive experience of plant employees.

Interviews were conducted on location in July 1981. All permanent employees whose jobs had ever taken them into the production areas of the plant on a regular basis were invited to participate. Reproductive history questionnaires (appended) were administered to 207 persons, including 10 who had worked in the nitrations or reductions areas of the plant, but were not available for the July interviews. These were reached by telephone over the next two months, thus ensuring that current employees who had ever worked in nitrations or reductions (except one who was out of state for the summer) were given the opportunity to be interviewed. In all, 14 eligible persons (six percent) were not interviewed; 4 refused and 10 were absent due to vacation, sickness, disability, or personal or company business. Among those interviewed five male employees and one of fifteen female employees had never married, and therefore, did not contribute to the analysis. Of 55 persons who had ever worked in the reductions area, 53 were interviewed (96 percent); similarly, 53 persons were interviewed of 55 who had ever worked in nitrations.

The five production areas of the plant are noted in Figure 1: (1) nitrations - includes offsites (loading methylene bisphenyl isocyanate: receiving benzene, toluene, ammonia, and other raw materials), sulfuric acid concentration, and the manufacture of nitric acid, dinitrotoluene, and nitrobenzene;

(2) reductions - includes the manufacture of toluene diamine, aniline (the "old aniline plant", which is currently used for reworking aniline), and diphenylamine; (3) toluene diisocyanate (TDI) - includes the manufacture of phosgene and TDI; (4) methylene bisphenyl isocyanate (MDI) - the manufacture of MDI and variants; and (5) aniline/nitrobenzene - the manufacture of nitrobenzene and aniline. Except for MDI, which is handled by nitrations personnel, areas load their own products. Persons assigned to an area rotate through all activities in the area according to a two week or a one month rotation schedule. The only significant exposures to dinitrotoluene occur in the nitrations area; likewise, the only significant exposures to toluene diamine occur in reductions.

The basic fertility analysis has used the method of Levine et al.[2-4] Job titles and dates comprising in-plant occupational histories for all employees were provided by the plant personnel office.

Pertinent results are displayed in the appended tables. Table 1, entitled "Married Fertility", describes fertility during periods in which employees were married and not permanently separated. Observed and expected births and the resulting ratio or standardized fertility ratio (SFR) are recorded for different slices of group reproductive experience. Pre-employment fertility is set forth in the pair of numerical columns at farthest left. Five other pairs of columns display post-employment fertility according to whether there were little or no opportunity for exposure ("None") -- e.g. layoff or other absence, administrative and certain technical jobs; opportunity for exposures in the nitrations area; for exposures in reductions; for multiple exposures not limited to one production area, as with various maintenance, laboratory, and technical positions; or "Other" exposures, referring to the experience of

individuals assigned to work in discrete production areas of the plant besides nitrations and reductions (including the nitric acid manufacturing facility, when denoted as such, and the TDI, MDI, and aniline/nitrobenzene production areas).

In the absence of plant chemical exposure the fertility of male employees ever assigned to the nitrations area (nitrations-exposed) does not differ from their fertility during periods at risk from nitrations exposures: Pre-employment + None SFR = 1.99 (76/38.1) vs. Nitrations SFR = 2.00 (17/8.5). The ratio of exposed to nonexposed SFRs (or θ) is 1.00, with 90% confidence limits 0.61 - 1.59, indicating that similar exposures in another chemical plant would not be expected to educe fertility by more than 39 percent or to cause an increase of more than 59 percent. Likewise, the fertility of employees who have ever worked in reductions (reductions-exposed) remains unaffected during periods at risk from reductions exposures: Pre-employment + None SFR = 2.01 (55/27.3) vs. Reductions SFR = 2.01 (32/15.9). The ratio of reductions to non-exposed SFRs (or θ) is 1.00, with 90% confidence limits 0.67 - 1.47.

Degree of exposure in nitrations or reductions was estimated by duration of employment in those areas and by exposure intensity designations assigned to each job title according to estimation of exposure potential by the plant industrial hygienist. Computer capability was developed to subdivide the reproductive experience of an individual, if necessary, and assign one portion to one exposure category (e.g. the first 2.0 years of reductions-related experience or reductions-related experience with high intensity exposure) and another portion to another exposure category (e.g. reductions-related experi-

ence subsequent to the first 2.0 years of reductions-related experience with low intensity exposure). Categories of duration of exposure were constructed so as to subdivide nitrations-related and reductions-related births into groups with at least 3.0 expected births, the minimum needed to confer sufficient stability to SFRs.

The following jobs were designated to confer the potential for high intensity exposure: productions technician, junior productions technician, temporary productions technician, laboratory technician, junior laboratory technician, laboratory trainee, chemical analyst, and temporary trackman (loader). Foreman, shift foreman, production shift supervisor, chemist, control chemist, senior development chemist, instrument technician, junior instrument technician, senior instrument technician, and senior development technician - all were considered to afford opportunity for medium intensity exposure. Several jobs were thought to be virtually without exposure: general production superintendent, production manager, isocyanate production manager, chief chemist, maintenance manager, instrument supervisor, engineering manager, chief project engineer, project engineering supervisor, process engineering supervisor, technical manager, production statistician, industrial relations supervisor, and secretary. The remaining positions were characterized by low intensity exposure. These included all safety and inspection jobs, all other engineering department titles, technical assistant, commissioning manager, maintenance engineer, general foreman (maintenance), laboratory supervisor, senior productions technician, area superintendent, pure and variants supervisor, and production day foreman.

Since experienced employees may be promoted to jobs of greater responsibility and less intense exposure, employees with the greatest duration of exposure in a particular area often will have jobs which involve the least intensity of exposure. In order to assess the effects of degree of exposure properly, therefore, it is necessary to stratify exposure intensity by duration. (Computer capability to permit stratification of exposure duration by intensity has not yet been developed). This was possible for high intensity exposure in nitrations or reductions, since categories of less than or equal to and more than 2.0 years exposure contain a minimum of 3.0 expected births. The results are presented in Table 2. Duration of employement in nitrations or reductions had no significant effect on the fertility of men exposed at high intensities; in fact, SFRs increased with greater duration of employment!

Persons who had held both salaried and hourly jobs were assigned both to salaried and hourly categories and separately to the hourly/salaried group (Table 1). Pre-employment fertility and weighted average ages of wives during the pre-employment period were similar for hourly and salaried employees; therefore, these groups were combined for subsequent analyses.[4]

Exposure-related fertility among female employees was insufficient to analyze.

Information about abnormalities or birth defects was elicited from the questions "Did any of your wife's children have an abnormality or defect?" and "What was the abnormality or defect?" The questions did not require the informant to decide if abnormalities or defects had been present at birth since problems first noted years later might not have been identified as resulting

from birth defects. Neonatal deaths were detected from responses to the questions: "Are all of your wife's children living?" and "When did he/she die?" The queries "Has your wife ever had a miscarriage or a stillborn child?" followed by "When was the (miscarriage or stillbirth)?" and "How many months pregnant was she at the time?" were used to establish and describe these events.

Inquiries were specifically directed at pregnancies terminated by medical or surgical means which did not result in a live birth - e.g. tubal pregnancies, elective induced abortions, and intrauterine fetal deaths where labor was induced by a physician. Such pregnancy outcomes may or may not have been included in responses to questions on miscarriages and stillbirths; however, the frequency of these events is not expected to differ with chemical exposure. Three pregnancies conceived in wedlock were reported to have been terminated by medical or surgical means. One was conceived during nitrations exposure; two, during exposures in production areas besides nitrations and reductions. Marital and exposure status of two other such pregnancies was not indicated.

Data on abnormalities and defects in liveborn offspring of the wives of male employees have been summarized in Table 3. There are no significant aggregations of abnormalities or defects with chemical exposure; nor are there two or more cases of a single well-defined birth defect occurring within any one exposure category. The two instances of abnormalities or defects ascribed to prematurity, both conceived during reductions exposure, were neonatal deaths.

The distribution by exposure of miscarriages, stillbirths, neonatal deaths, and live births conceived in wedlock by the wives of male employees has been enumerated in Table 4. The number of reported pregnancies at risk is probably somewhat less than the true figure. This is because pregnancies conceived within nine months of the date of interview that result in miscarriages, stillbirths, or neonatal deaths (the majority of whom have been prematurely born) are more likely to conclude prior to interview than those which result in the birth of living infants.

For purposes of analysis miscarriages, stillbirths, and neonatal deaths have been grouped together. This arrangement makes good sense if one considers that the most likely hypothesis to explain an effect on the male leading to an adverse reproductive outcome besides diminished capacity to achieve conception would involve chromosomal damage or a genetic mutation. Such an event could lead to a birth defect, which if severe enough might result in a spontaneous abortion, a stillbirth, or a neonatal death. One can easily discern in Table 4 that for all males there is no significant clustering of adverse reproductive outcomes with nitrations or reductions exposure. This becomes even more evident after excluding the reproductive experience of habitual aborters, defined as women for whom three consecutive pregnancies have resulted in miscarriage, stillbirth, or neonatal death due to prematurity. These women are more likely to have constitutional abnormalities, which can account for their adverse reproductive outcomes.

In summary, the analysis of reproductive experience at Rubicon Chemicals' Geismar, Louisiana plant has revealed no evidence for a decrease in fertility

related to working in the nitrations or reductions areas, where exposures to dinitrotoluene and toluene diamine may occur. Moreover, there was no evidence in these areas of an abnormal aggregation of miscarriages, stillbirths, neonatal deaths, or birth defects.

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Figure 1

RUBICON PRODUCTION AREAS

NITRATIONS	AMMONIA → NITRIC ACID TOLUENE → DINITROTOLUENE BENZENE → NITROBENZENE SULFURIC ACID CONCENTRATION OFFSITES
REDUCTIONS	DINITROTOLUENE → TOLUENE DIAMINE NITROBENZENE → ANILINE ANILINE → DIPHENYLAMINE
TDI	TOLUENE DIAMINE → TDI CARBON MONOXIDE + CHLORINE → PHOSGENE
MDI	ANILINE → DADPM → MDI MDI (POLY) → PURE MDI → VARIANTS
ANILINE/NITROBENZENE	BENZENE → NITROBENZENE NITROBENZENE → ANILINE

Table 1
MARRIED FERTILITY+

Group	Pre-Employment O/E	Pre-Employment SFR	Post-Employment Exposures: None O/E	None SFR	Nitrations O/E	Nitrations SFR	Reductions O/E	Reductions SFR	Multiple O/E	Multiple SFR	Other O/E	Other SFR
All employees	273/126.0	2.17	11/3.3	3.33	17/8.6	1.98	32/16.1	1.99	38/18.2	2.09	34/19.7	1.73
All males	252/116.8	2.16	8/2.1	3.81	17/8.5	2.00	32/15.9	2.01	38/17.9	2.12	34/19.5	1.74
White	219/100.5	2.18	8/2.1	3.81	10/5.6	1.79	30/13.6	2.21	30/15.0	2.00	28/16.0	1.77
Non-white	33/ 16.3	2.02	0/0.0	----	7/2.9	2.39	2/ 2.2	0.89	8/ 2.9	2.76	6/ 3.4	1.76
Spanish surname	3/ 0.5	5.75	0/0.0	----	0/0.2	0.00	-------	----	-------	----	0/ 0.2	0.00
Hourly	198/ 96.1	2.06	3/1.2	2.50	17/8.4	2.02	31/15.5	2.00	26/12.4	2.10	34/19.4	1.75
Salaried	97/ 41.8	2.32	7/1.5	4.67	7/ 3.8	1.84	11/ 6.0	1.83	26/11.9	2.18	5/ 6.6	0.76
Hourly/salaried	43/ 21.1	2.04	2/0.5	4.00	7/ 3.7	1.89	10/ 5.6	1.79	14/ 6.4	2.19	5/ 6.5	0.77
Nitrations-exposed	75/ 37.7	1.99	1/0.4	2.50	17/ 8.5	2.00	7/ 3.3	2.12	5/ 2.3	2.17	9/ 5.9	1.53
Reductions-exposed	55/ 27.1	2.03	0/0.2	0.00	2/ 1.0	2.00	32/15.9	2.01	8/ 3.2	2.50	11/ 5.1	2.16
≤ 2.0 years exposure					8/ 4.5	1.77	16/ 6.6	2.41				
> 2.0 years exposure					9/ 4.0	2.27	16/ 9.2	1.74				
Low intensity exposure					3/ 0.7	4.39	3/ 3.4	0.89				
Medium intensity exposure					0/ 0.5	0.00	2/ 1.0	1.93				
High intensity exposure					14/ 7.2	1.93	27/11.4	2.36				
All females	21/ 9.2	2.28	3/1.2	2.50	0/ 0.3	0.00	0/ 0.2	0.00	0/ 0.2	0.00	0/ 0.4	0.00

O/E - observed/expected births; SFR - standardized fertility ratio; Nitrations - includes loading MDI, unloading raw materials, and the following manufacturing processes: nitric acid, dinitrotoluene, and nitrobenzene; Reductions - includes the manufacture of toluene diamine, aniline, and diphenylamine; Multiple - persons who are not assigned to a particular area, such as with various maintenance, laboratory, and technical jobs; Other - persons assigned to other discrete areas of the plant with the following manufacturing processes: toluene diisocyanate, diphenylmethane diisocyanate and variants, nitrobenzene, aniline, and the old nitric acid plant; No exposure - layoff or other absence, administrative and certain technical job categories.

+ Expected births were rounded to the nearest tenth.

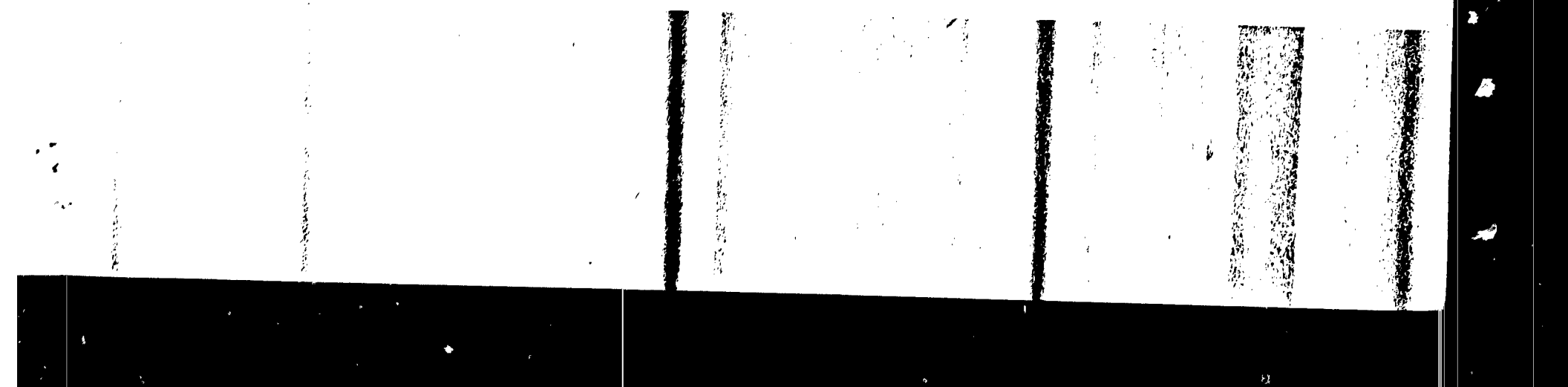

Table 2

HIGH INTENSITY EXPOSED MALES:
MARRIED FERTILITY BY DURATION OF EXPOSURE

Group	Nitrations		Reductions	
	O/E	SFR	O/E	SFR
≤ 2.0 years exposure	8/4.2	1.89	14/6.2	2.27
> 2.0 years exposure	6/3.0	2.00	13/5.3	2.47

Table 3

ABNORMALITIES OR DEFECTS REPORTED IN LIVEBORN OFFSPRING

MALES, MARRIED EXPERIENCE

Group	Number with Abnormalities / Defects	Live Births	Ratio
All males			
Pre-Employment	26	252	0.10
Post-Employment	16	129	0.12
No Exposure	0	8	0.00
Nitrations Exposure	2	17	0.12
Reductions Exposure	6	32	0.19
Multiple Exposure	5	38	0.13
Other Exposure	3	34	0.09

LIST OF ABNORMALITIES AND DEFECTS: P-110 MALES,
LIVEBORN OFFSPRING OF POST-EMPLOYMENT MARRIED EXPERIENCE

anencephaly
heart murmur, jaundice, pneumonia, prematurity
*heart murmur (disappeared at 18 mos.), corrective shoes
open chest (no sternum), corrective shoes
+birth mark on back
*dyslexia
*jaundiced at birth
*hearing problems
*prematurity
*prematurity
multiple congenital defects
+hypospadias
pupil of one eye shaped like a key
small fingers on one hand
cross-eyed, nearsighted, dyslexia
kidney reflux

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*child conceived during reductions exposure

+child conceived during nitrations exposure

Table 4

MISCARRIAGES, STILLBIRTHS, NEONATAL DEATHS: MALES, MARRIED EXPERIENCE

Group	Miscarriages + Stillbirths by Trimester 1	2	3	Neonatal Deaths	Live Births	Miscarriages+Stillbirths+Neonatal Deaths Total Pregnancies Number	Percent
All males							
Pre-Employment	25+	5	3	5	252	38/285	13
Post-Employment	19+	4	3	3	129	29/155	19
No Exposure	0	0	0	0	8	0/ 8	0
Nitrations Exposure	2	1	0	0	17	3/ 20	15
Reductions Exposure	3	2	0	2	32	7/ 37	19
Multiple Exposure	7+	0	2	1	38	10/ 47	21
Other Exposure	7*	1	1	0	34	9/ 43	21
All males (excludes habitual aborters)							
Pre-Employment	21+	4	1	5	247	31/273	11
Post-Employment	16*+	2	3	1	123	22/144	15
No Exposure	0	0	0	0	8	0/ 8	0
Nitrations Exposure	2	1	0	0	17	3/ 20	15
Reductions Exposure	2	0	0	0	28	2/ 30	7
Multiple Exposure	7+	0	2	1	38	10/ 47	21
Other Exposure	5*	1	1	0	32	7/ 39	18

* Includes one miscarriage conceived less than nine months from the date of interview

+ Includes one tubal pregnancy

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August 17, 1981

James Hathaway, M.D., M.P.H.
Medical Director: Chemicals
Allied Chemical Corporation
P.O. Box 1057-R
Morristown, NJ 07960

Dear Dr. Hathaway:

The analysis of fertility at Allied's Moundsville, WV plant has been completed. I expect to mail you under separate cover within the next ten days the results of the miscarriage, stillbirth, and birth defect data.

There is no evidence of a decrease in fertility related to exposure to dinitrotoluene or other agents in Building 55. Nor is there convincing evidence of a decrease in fertility related to exposure to toluene diamine or other agents in Building 52.

The study has proceeded according to the method I have presented in my recent articles and letter in the Journal of Occupational Medicine. It is based on interviews conducted by my staff towards the end of April 1981. Job titles and dates comprising in-plant occupational history were provided by the plant personnel and safety offices and were reviewed for accuracy with employees. Where there were conflicting opinions, the dates and job titles given by the employees were used in preference to those provided by plant management; however, in general, there was good agreement between management and employees about these matters.

I am grateful for the excellent response of your employees toward this study and to Mr. Higgins and Mr. Callow in particular--without their willing and knowledgeable assistance the study could not have been completed. A total of 268 persons--everyone whose job had ever taken him into the exposure areas of the plant on a regular basis--were invited to participate in the study. This included all hourly employees and 48 of 76 salaried staff. Persons who had worked only in the administrative offices were excluded from the study as were temporary or contract personnel. Interviews were obtained from 235 individuals, including five hourly employees who had worked in Buildings 52 or 55, but who had been absent during the April interviews. These were interviewed in May by telephone. All hourly employees who had ever worked in Buildings 52 (TDA) or 55 (DNT) were given the opportunity to participate. In sum 33 eligibles were not interviewed: 7 refused and 26 were absent as the result of vacation, sickness, accident, or long-term disability. Only

two persons (refused) were not interviewed from among 45 male employees who had ever worked in Building 52 (TDA); likewise, of 32 males who had ever worked in Building 55 (DNT), only one person (refused) was not interviewed. Ten participants had never been married and thus did not contribute to the analysis. The preponderance (213) of ever-married participants were white males. There were 3 non-white males and 9 females.

Pertinent results are displayed in the appended tables. The table entitled "Married Fertility: P-100" describes fertility during periods in which employees were married and not permanently separated. Observed and expected births and the resulting ratio or standardized fertility ratio (SFR) are recorded for different slices of group reproductive experience. Pre-employment fertility is set forth in the pair of numerical columns at farthest left. Five other pairs of columns display post-employment fertility according to whether there was little or no opportunity for exposure ("None")--e.g. layoff, leave of absence, Buildings 44 (power house) or 61 (refrigeration); opportunity for exposures in Buildings 55 (DNT) or 52 (TDA); for plantwide or multiple exposures (the "Multiple" column) such as might be encountered by maintenance or laboratory personnel and loaders; or "Other" exposures, referring to the experience of individuals assigned to work in discrete areas of the plant besides Buildings 55 or 52.

As I have discussed especially in my recent letter to the editor of the Journal of Occupational Medicine, there is a small artifactual tendency for married fertility after employment to be reduced in comparison with pre-employment fertility (or for no-exposure fertility, consisting of the sum of pre-employment and post-employment "None" experience, to exceed post-employment exposed fertility). This is because the U.S. general population from which expected births for the plant population are derived will contain a greater proportion of married women at older ages; and workers are indeed older after employment (exposure) than before. Plant observed fertility, on the other hand, is based only on married years. For example, the weighted average age of the wives of all males in the pre-employment category is 26 (or 27 for the total period of no exposure as defined above). Corresponding weighted average ages for post-employment exposure categories range from 32-37, thereby resulting in a six (eight) percent increase in the proportion married among the general population compared to no-exposure (pre-employment) periods. Post-employment standardized fertility ratios, therefore, would be expected to be approximately six (eight) percent lower than corresponding rates during the period of no exposure (pre-employment).

Keeping this in mind, the pattern of fertility for male employees can be interpreted. DNT or "Other" exposure-related fertility, if anything, is probably slightly higher than no-exposure or pre-employment fertility. Fertility for the post-employment exposure categories "None," "TDA," and "Multiple" is somewhat lower than expected. Within TDA-exposed males, TDA-exposure related fertility remains less than corresponding fertility during no-exposure periods. The analysis of fertility based on the table entitled "Married Fertility: P-100," however, deals with aggregate fertility during different exposure periods. It assumes that the underlying fertility of the group does not vary with female age, birth cohort, or parity or that the distribution of these parameters is similar across exposure periods. The parameter with greatest impact on fertility is parity.

The relationship of parity to fertility among P-100 males is set forth in the tables entitled "Married Fertility by Parity: P-100 Males" and "Married Fertility by Parity: P-100 TDA-Exposed Males by Degree of Exposure." From the first of these tables it can be readily discerned that fertility is not constant across parity levels and declines as parity rises. This is evident from a scrutiny of parity-specific SFRs for all males during the pre-employment period, when fertility is unlikely to be confounded by differences in environmental exposures. The greatest decrement in fertility occurs between Parity 0 and 1 and may be attributed to the preponderance of nulliparous single women in the general population depressing the expected number of births at Parity 0. At higher parities [illegible] continue to decline, although at a much slower rate.

For all parities except Parity 3 parity-specific SFRs are greater during the period of TDA exposure than prior to employment at the plant. This is true whether examining the fertility of all males or only that of male employees who have been exposed to TDA. The fact that aggregate fertility prior to employment seems to exceed fertility during exposure to TDA is accounted for by the much greater contribution of Parity 0 to pre-employment fertility. Sixteen percent of all male expected births for the pre-employment period occurred at Parity 0 compared to seven percent of expected births during TDA exposure. Since Parity 0 SFRs are characteristically large, the greater contribution of this parity level to aggregate fertility during the pre-employment period increases the overall pre-employment SFR.

In order to account for differences in the contributions of various parities to aggregate fertility during exposure periods, parity-specific expected births were adjusted as follows: Post-employment fertility at no risk from exposure to DNT or TDA (exposures "None" or "Other") was used as a baseline. At each parity level the number of expected births was adjusted by multiplying by the baseline parity-specific SFR divided by the baseline SFR at Parity 2. In this way baseline SFRs at other parities were converted to the baseline SFR at Parity 2. Assuming that the factors governing the divergence of parity-specific SFRs of the baseline are the same as those operating during other exposure periods, such an adjustment would produce aggregate SFRs unencumbered by differences in the contributions of various parity levels.

The table entitled "Parity-Adjusted Married Fertility: P-100 Males" displays the results of adjusting aggregate SFRs as described. The standard against which to compare adjusted SFRs is the adjusted SFR for "No Exp. + Other Exp." (baseline). The change in fertility with exposure is denoted by θ and is simply the ratio of adjusted SFRs of a given exposure period with baseline. In all cases post-employment adjusted SFRs exceed pre-employment values, and DNT-related SFRs exceed baseline. For all males, fertility during the post-employment periods "No Exposure", "TDA Exposure", and "Multiple Exposure" is less than baseline, but differences are not statistically significant and may result from random variation. Restricting the analysis to TDA-exposed males has the advantage of examining the same persons under different conditions of exposure, but the disadvantage of smaller numbers with greater attendant instability. Adjusted fertility related to TDA exposure of TDA-exposed males is virtually identical to baseline. The 90% confidence limits on θ indicate that the data available from the plant for exposure areas of concern - DNT, TDA, and Multiple Exposure - would have been sufficient at least to detect with 90% certainty a reduction in fertility of 60 - 80 percent (θ = 0.40 - 0.20) as occurred among workers exposed to dibromochloropropane (DBCP) at a California pesticide plant.

Degree of exposure to TDA was estimated by duration of exposure and by exposure intensity designations assigned to each job title by Mr. Higgins, Manager of Safety and Environment, according to his estimation of exposure potential. Computer capability was developed to subdivide the reproductive experience of an individual, if necessary, and assign one portion to one exposure group (e.g. the first 1.5 years of TDA exposure or TDA exposure as a helper) and another portion to another exposure group (e.g. TDA exposure subsequent to the first 1.5 years or TDA exposure as a foreman). Duration of exposure categories of less than 1.5 years or greater than/equal to 1.5 years were constructed in order to subdivide TDA-related expected births equally. The following job titles were linked to exposures of lesser intensity: laborer-janitor, operator prior to November 15, 1972, unit foreman, shift foreman, acting/temporary assistant foreman. Greater intensity exposures were assigned to helper, Building 52 designated laborer, and operator on/after November 15, 1972. (Operator and helper classifications were merged into a single operator category in November 1972.)

Greater degree of exposure to TDA was associated with reduced fertility with or without parity adjustment. The reductions observed in fertility cannot be explained by differences in weighted average age of wives between exposure groups (weighted average ages 28 and 33 for less than or greater than/equal to 1.5 years exposure, respectively; 32 for both intensity of exposure groups).

Of 42 male employees who had ever worked in Building 52, only one admitted to trying for a year or more to achieve a pregnancy without success beginning during the period of TDA exposure. This compares to one of 47 male employees producing the food additives malic and fumaric acids who reported a lack of success which began during the period of exposure to these acids. Both exposure periods are of comparable size in terms of numbers of births expected: 7.6 and 7.5, for TDA and malic/fumaric acids, respectively.

Persons who had held both salaried and hourly jobs were assigned both to salaried and hourly categories and separately to the hourly/salaried group. Pre-employment fertility and weighted average ages of wives during the pre-employment period are almost identical for hourly and salaried employees. There is, therefore, no difficulty in disregarding these categories in relation to fertility.

Exposure-related fertility among female employees was insufficient for analysis.

In summary, there is no evidence of a decrease in fertility related to exposure to dinitrotoluene or other agents in Building 55; nor is there convincing evidence of a decrease in fertility related to exposure to toluene diamine or other agents in Building 52. Fertility related to TDA exposure of TDA-exposed males is virtually identical to the post-employment fertility of these individuals during periods which preclude exposure to DNT or TDA ("No Exposure" and "Other Exposure"). Post-employment fertility of all male employees during such periods exceeds TDA-related fertility; but whether this is due to random variation or reflects a biological effect of occupational exposure cannot be determined with assurance. Indeed, the possibility for variation unrelated to occupational exposure to have influenced the outcome is more likely here since the exposure groups being compared include different individuals. It should be noted that the post-employment fertility of all male employees during

periods which preclude exposure to DNT or TDA exceeds to the same extent post-employment fertility during periods lacking any chemical exposure. Moreover, the incidence of noticeable fertility problems beginning during the period of TDA exposure seems not to differ from the incidence of such problems during exposure to chemicals of no concern. Nevertheless, the suggestion of a dose-response relationship between fertility and degree of exposure in Building 52, although not statistically significant, holds open the possibility that a mild reduction in fertility related to occupational exposures in this area may have taken place.

Please let me know if you require additional information or explanation. With many thanks for your generous assistance.

Yours truly,

Richard J. Levine, M.D.
Chief of Epidemiology

cc: Dr. Robert A. Neal, President
Dr. James E. Gibson, Director of Research

MARRIED FERTILITY: P-100+

Group	Pre-Employment		Post-Employment									
			Exposures									
			None		DNT		TDA		Multiple		Other	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
All employees	321/173.1	1.85	15/9.9	1.52	11/6.2	1.76	11/7.6	1.45	90/56.9	1.58	96/52.7	1.82
All males	301/163.6	1.84	13/9.0	1.44	11/6.2	1.76	11/7.6	1.45	90/56.9	1.58	96/52.7	1.82
White	294/160.6	1.83	13/9.0	1.44	11/6.2	1.76	10/7.5	1.33	90/56.8	1.58	96/52.5	1.83
Non-white	7/ 3.0	2.32	0/0.0	0.00	------	----	1/0.1	10.00	0/ 0.1	0.00	0/ 0.2	0.00
Spanish surname	5/ 1.9	2.62	0/0.1	0.00	------	----	0/0.2	0.00	1/ 1.0	1.00	4/ 2.2	1.82
Hourly	275/149.6	1.84	10/7.3	1.37	11/6.2	1.76	11/7.6	1.45	82/53.6	1.53	94/52.6	1.79
Salaried	69/ 37.3	1.85	5/4.0	1.25	1/1.2	0.83	5/3.6	1.39	25/13.8	1.81	21/10.2	2.06
Hourly/salaried	43/ 23.3	1.84	2/2.4	0.83	1/1.2	0.83	5/3.6	1.39	17/10.4	1.63	19/10.0	1.90
TDA-exposed males	41/ 23.8	1.72	0/0.7	0.00	3/0.5	6.31	11/7.6	1.45	17/7.6	2.24	14/8.6	1.63
<1.5 years exposure							8/3.9	2.05				
≥1.5 years exposure							3/3.6	0.83				
Lesser intensity							5/2.9	1.72				
Greater intensity							6/4.6	1.30				
All females*	20/ 9.5	2.11	2/1.0	2.00	0/0.0	0.00	0/0.0	0.00	0/0.0	0.00	0/0.1	0.00

O/E - observed/expected births; SFR - standardized fertility ratio; DNT - Building 55; TDA - Building 52; Multiple exposures - persons who cannot be assigned to a particular area, such as plantwide maintenance, loaders, and laboratory personnel; Other exposures - Buildings 31, 35, 41, 42, 43, 53, 57, 63, 65, 66, 67, and SAC; No exposure - layoff or leave of absence, Buildings 44, 61

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* All females were white and hourly employees; one had been both an hourly and a salaried employee.

+ Expected births were rounded to the nearest tenth.

MARRIED FERTILITY BY PARITY: P-100 MALES+

Group	Pre-Employment		Post-Employment									
			Exposures									
			None		DNT		TDA		Multiple		Other	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
All males	301/163.6	1.84	13/9.0	1.44	11/6.2	1.76	11/7.6	1.45	90/56.9	1.58	96/52.7	1.82
Parity 0	135/ 26.0	5.19	2/0.6	3.33	0/0.1	0.00	3/0.5	6.00	16/ 3.0	5.33	21/ 2.2	9.55
Parity 1	98/ 76.1	1.29	5/4.1	1.22	3/1.1	2.73	3/2.1	1.43	26/16.7	1.56	31/17.0	1.82
Parity 2	48/ 39.2	1.22	3/1.6	1.88	3/2.4	1.25	4/2.8	1.43	20/17.4	1.15	24/15.8	1.52
Parity 3	13/ 15.5	0.84	2/1.9	1.05	4/1.0	4.00	0/1.6	0.00	20/10.8	1.85	12/10.3	1.17
Parity 4+	7/ 6.9	1.01	1/0.8	1.25	1/1.6	0.63	1/0.5	2.00	8/ 9.5	0.84	8/ 7.5	1.07
TDA-exposed males	41/ 23.8	1.72	0/0.7	0.00	3/0.5	6.31	11/7.6	1.45	17/ 7.6	2.24	14/ 8.6	1.63
Parity 0	22/ 4.4	5.00	0/0.0	0.00	0/0.1	0.00	3/0.5	6.00	2/ 0.4	2.50	6/ 0.7	8.57
Parity 1	13/ 12.8	1.02	0/0.4	0.00	0/0.0	0.00	3/2.1	1.43	7/ 3.1	2.26	4/ 2.5	1.60
Parity 2	6/ 5.2	1.15	0/0.0	0.00	2/0.3	6.67	4/2.8	1.43	3/ 2.2	1.36	2/ 2.7	0.74
Parity 3	0/ 1.4	0.00	0/0.2	0.00	1/0.1	10.00	0/1.6	0.00	5/ 1.0	5.00	1/ 1.5	0.67
Parity 4+	0/ 0.0	0.00	0/0.0	0.00	0/0.0	0.00	1/0.5	2.00	0/ 0.8	0.00	1/ 1.0	1.00

O/E - observed/expected births; SFR - standardized fertility ratio; DNT - Building 55; TDA - Building 52; Multiple exposures - persons who cannot be assigned to a particular area, such as plantwide maintenance, loaders, and laboratory personnel; Other exposures - Buildings 31, 35, 41, 42, 43, 53, 57, 63, 65, 66, 67, and SAC; No exposure - layoff or leave of absence, Buildings 44, 6[illegible]

+ Expected births were rounded to the nearest tenth.

MARRIED FERTILITY BY PARITY: P-100 TDA-EXPOSED MALES BY DEGREE OF EXPOSURE+

	<1.5 Yrs. Exposure		≥1.5 Yrs. Exposure		Lesser Intensity		Greater Intensity	
Group	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
Parity 0	3/0.4	7.50	0/0.1	0.00	1/0.0	----	2/0.4	5.00
Parity 1	2/1.5	1.33	1/0.6	1.67	1/0.4	2.50	2/1.7	1.18
Parity 2	2/1.2	1.67	2/1.5	1.33	2/1.1	1.82	2/1.7	1.18
Parity 3	0/0.4	0.00	0/1.3	0.00	0/1.0	0.00	0/0.7	0.00
Parity 4+	1/0.4	2.50	0/0.2	0.00	1/0.4	2.50	0/0.1	0.00

O/E - observed/expected births; SFR - standardized fertility ratio; Lesser Intensity - the following job titles: laborer-janitor, operator prior to November 15, 1972, unit foreman, shift foreman, acting/temporary assistant foreman; Greater Intensity - the following job titles: operator on and after November 15, 1972 (when operator and helper classifications were merged), helper, Building 52 designated laborer

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+ Expected births were rounded to the nearest tenth.

PARITY-ADJUSTED MARRIED FERTILITY: P-100 MALES[+]

Group	O/E	SFR	p-value (one-tailed)	θ	90% Confidence Limits on θ
All males					
Pre-Employment	301/277.2	1.09	----	(0.70)	----------
Post-Employment					
No Exposure	13/ 11.3	1.15	0.19	0.74	(0.43, 1.23)
DNT Exposure	11/ 6.0	1.84	0.77	1.19	(0.65, 2.03)
TDA Exposure	11/ 9.3	1.18	0.24	0.76	(0.42, 1.30)
Multiple Exposure	90/ 66.3	1.36	0.19	0.88	(0.69, 1.12)
Other Exposure	96/ 59.1	1.63	0.66	1.05	(0.82, 1.33)
No Exp. + Other Exp.	109/ 70.3	1.55	----	(1.00)	----------
TDA-exposed males					
Pre-Employment	41/ 81.2	0.51	----	(0.69)	----------
Post-Employment					
No Exposure	0/ 0.9	0.00	0.52	0.00	(0.00, 4.98)
DNT Exposure	3/ 1.5	1.95	0.97	2.64	(0.64, 8.08)
TDA Exposure	11/ 14.6	0.76	0.61	1.03	(0.48, 2.14)
<1.5 yrs. exposure	8/ 9.5	0.84	0.71	1.14	(0.49, 2.56)
≥1.5 yrs. exposure	3/ 5.1	0.59	0.50	0.80	(0.20, 2.44)
Lesser Intensity	5/ 3.2	1.57	0.96	2.13	(0.74, 5.41)
Greater Intensity	6/ 10.2	0.59	0.42	0.80	(0.30, 1.92)
Multiple Exposure	17/ 14.5	1.17	0.93	1.59	(0.83, 3.10)
Other Exposure	14/ 18.1	0.78	0.63	1.05	(0.52, 2.10)
No Exp. + Other Exp.	14/ 19.0	0.74	----	(1.00)	----

+Designations according to preceding tables. Expected births were rounded to the nearest tenth. Within "All Male" and "TDA-Exposed Male" categories, the group Post-Employment No Exp. + Other Exp. was used as a baseline from which to adjust parity and to compute p-values, θs, and 90% confidence limits.

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August 25, 1981

James Hathaway, M.D., M.P.H.
Medical Director: Chemicals
Allied Chemical Corporation
P.O. Box 1057-R
Morristown, NJ 07960

Dear Dr. Hathaway:

The analysis of reported miscarriages, stillbirths, neonatal deaths, and birth defects at Allied's Moundsville, WV plant has been completed. There is no evidence of an abnormal aggregation of birth defects with chemical exposure. However, a cluster of miscarriages, stillbirths, and neonatal deaths conceived during the period of exposure to toluene diamine or other agents in Building 52 has been observed.

Many technical details of the study have been described in my letter of August 17. Information about abnormalities or birth defects was elicited from the questions "Did any of your wife's children have an abnormality or defect?" and "What was the abnormality or defect?" The questions did not require the informant to decide if abnormalities or defects had been present at birth since problems first noted years later might not have been identified as stemming from birth defects. Neonatal deaths were detected from responses to the questions: "Are all of your wife's children living?" and "When did he/she die?" The queries "Has your wife ever had a miscarriage or a stillborn child?" followed by "When was the (miscarriage or stillbirth)?" and "How many months pregnant was she at the time?" were used to establish and describe these events. Reported third trimester miscarriages or stillbirths were verified by asking respondents if the infant had been born dead. Inquiries were not specifically directed at pregnancies terminated by medical or surgical means which did not result in a live birth - e.g., tubal pregnancies, elective induced abortions, and intrauterine fetal deaths where labor was induced by a physician. Such pregnancy outcomes may or may not have been included in the responses to questions on miscarriages and stillbirths. Nevertheless, the frequency of these events is not expected to differ with chemical exposure.

Data on abnormalities and defects in liveborn offspring of the wives of male employees have been summarized in the tables entitled, "Abnormalities or Defects Reported in Liveborn Offspring: P-100 Males, Married Experience" and "List of Abnormalities and Defects: P-100 Males, Married Experience". It is evident that there is no aggregation either of total or cardiovascular abnormalities/defects with chemical exposure. (Cardiovascular abnormalities were examined separately since there were several of them). Nor are there two or more cases of a single well defined birth defect occurring within any one exposure category.

The distribution by exposure of miscarriages, stillbirths, neonatal deaths, and live births among the wives of male employees during married years has been enumerated in the table entitled, "Miscarriages, Stillbirths, Neonatal Deaths: P-100 Males, Married Experience". Two tubal pregnancies were identified and reported as miscarriages. The number of total pregnancies at risk recorded in the table is probably somewhat less than the true figure. This is because pregnancies terminated by medical or surgical means may or may not have been reported; and, in contrast to miscarriages and stillbirths, liveborn infants conceived within nine months of the date of interview would not have been born prior to interview.

One will readily observe that the number of miscarriages, stillbirths, and neonatal deaths relative to total reported pregnancies is in excess for the period of TDA exposure. Because this is true for males ever exposed to TDA as well as for all male employees, the cluster cannot be explained by a high rate of adverse reproductive outcomes occurring among the wives of males ever exposed to TDA regardless of chemical exposure. The six miscarriages, stillbirths, and neonatal deaths of the cluster were not due to the fortuitous presence of women who are chronic aborters since they were products of conceptions from six different women. Only one of these women had had an adverse pregnancy outcome on a prior occasion. (This was the mother of the neonate who died. She previously had given birth to another child who died during the neonatal period!) Using chi square with one degree of freedom and the Yates correction for continuity, the number of adverse reproductive events occurring during TDA exposure relative to pregnancies at risk is significantly greater than during the post-employment experience of all male employees under conditions of "no exposure" or "other exposure": 6/16 vs. 10/118, $p = 0.003$. All but one of these events occurred after the first trimester of pregnancy, whereas usually first trimester miscarriages would be expected to predominate. During the all male multiple exposure category the frequency of adverse pregnancy outcomes is also increased and skewed toward later trimesters. While this is not statistically significant, it is compatible with the hypothesis that an exposure in the TDA area plays a role in the production of miscarriages, stillbirths, and neonatal deaths since TDA area exposures would be included in the multiple exposure category.

Persons exposed for longer durations or at greater intensities would be expected to enhance their risk of adverse pregnancy outcomes if TDA area exposures of male employees were indeed involved in producing miscarriages, stillbirths, and neonatal deaths. Thus fathers of conceptions during the period of TDA exposure which had unfavorable outcomes would be expected to have received greater exposure by the time of conception than fathers of children conceived during TDA exposure who survived the neonatal period. However, no substantial difference can be found. The median duration of uninterrupted TDA exposure at conception of an adverse reproductive event was 1.1 years compared to 0.9 years at conception of a child surviving the neonatal period. Using a scale of intensity of exposure constructed by Mr. Higgins, job titles held by male employees at the time of conception during TDA exposure were ranked from low (1) to high (4) as follows: janitor-laborer and shift foreman (1), operator (2), operator after November 1972 (3), and helper (4). The intensity of exposure of fathers at the time of conception of children who survived

the neonatal period was similar to the intensity of exposure at conception of miscarriages, stillbirths, and neonatal deaths (mean score 2.9 vs. 2.5, respectively). Taking into account exposure duration and intensity and using personal knowledge of individuals to assist with the exposure rating, Mr. Higgins and his staff assigned a qualitative level of exposure (low, medium, high) during work in the TDA area to each man who had ever worked there. Again there was little difference between the groups. Of fathers of children surviving the neonatal period, one was ranked high; five were moderate; and four, low. Three fathers of adverse pregnancy outcomes were considered low; and three, moderate.

An effect of TDA exposure on male reproductive capacity could persist for an uncertain length of time after exposure has ceased. Under such circumstances, one might expect to find abnormalities in the subsequent reproductive experience of TDA-exposed workers. However, this seems not to be so. Following TDA area exposure, but not including periods of multiple exposure since TDA area exposures are encountered in the multiple exposure category, ten births and one miscarriage occurred to the wives of workers ever exposed to TDA. The ratio of miscarriages, stillbirths, and neonatal deaths to total reported pregnancies (1/11 = 0.09) is similar to the ratio obtained from post-employment "no exposure", "DNT exposure", and "other exposure" categories of TDA-exposed males prior to TDA exposure (1/8 = 0.13). The single miscarriage after TDA exposure did not occur in one of the six women who had conceived pregnancies with adverse outcomes during the period their husbands were employed in Building 52. Subsequent to TDA exposure, the fertility of these six women appears to be normal, with 3 births, 0 miscarriages/stillbirths/neonatal deaths, and 2.3 expected births after adjustment by the method outlined in my letter of August 17. This compares to 0 births, 1 miscarriage, and 1.4 expected births for women who had conceived only live births during the period of TDA area exposure.

In summary, there is no evidence of an abnormal aggregation of birth defects with chemical exposure. However, a cluster of miscarriages, stillbirths, and neonatal deaths conceived during the period of exposure to toluene diamine or other agents in Building 52 has been observed. Severity of exposure in Building 52 does not appear to be related to risk of an adverse pregnancy outcome; and the subsequent reproductive history of TDA-exposed men and the subgroup with TDA area-related miscarriages, stillbirths, or neonatal deaths seems to be normal after leaving Building 52.

An excess of miscarriages among wives of workers exposed to dinitrotoluene and toluene diamine at another chemical plant has been suspected in the report of a plant health hazard evaluation undertaken by NIOSH (HE 79-113-728). If one, however, excludes the reproductive experience of the exposed individual whose wife appears to be a chronic aborter and who apparently requested the plant evaluation, the rate of miscarriages among exposed employees seems no different from controls. Nevertheless, with this background in mind, the finding of a cluster of adverse pregnancy outcomes during TDA area exposure deserves further scrutiny.

CIIT would be interested to obtain medical records of hospitalizations and medical visits related to the miscarriages, stillbirths and neonatal deaths reported in this study. An examination of such records would be extremely useful in deciding whether the cluster of adverse pregnancy outcomes observed during TDA area exposure were likely to be related to occupational or non-occupational causes. We would also welcome participation in continued reproductive surveillance of men who have worked in Building 52 or in any capacity that you suggest.

Please let me know if you require additional information or explanation.
With best wishes,

Yours truly,

Richard J. Levine, M.D.
Chief of Epidemiology

cc: Dr. Robert A. Neal, President
Dr. James E. Gibson, Director of Research

ABNORMALITIES OR DEFECTS REPORTED IN LIVEBORN OFFSPRING:
P-100 MALES, MARRIED EXPERIENCE

Group	Number with (Cardiovascular) Abnormalities / Defects	Live Births	Ratio
All males			
Pre-Employment	17 (4)	301	0.06
Post-Employment			
No Exposure	1 (0)	13	0.08
DNT Exposure	1 (1)	11	0.09
TDA Exposure	0 (0)	11	0.00
Multiple Exposure	7 (2)	90	0.08
Other Exposure	9 (1)	96	0.09

LIST OF ABNORMALITIES AND DEFECTS:
P-100 MALES, MARRIED EXPERIENCE

slow learner
asthma, hay fever
small at birth
blood problem at birth
irregular heartbeat*
undescended testicle
one eye moved and quivered
heart partition didn't come together*
inner ear nerve damage
doctor broke back at delivery
inguinal hernia at birth
heart murmur, hole in the heart*
crossed eyes
hole in the heart*
mentally retarded, Mongoloid
hyperactive
Rh baby
weak eye after high fever
nervous condition of eye-rolling
slow heartbeat, needed pacemaker*
diabetic
cleft palate
lobe of one ear has a point
ruptured stomach wall
premature
one short leg
premature
premature
heart murmur*
transposition of main arteries of heart*
blind with cataracts at birth
allergic to foods; cyst in breast
congenital heart defect*
sterile
red mark on nose

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* cardiovascular abnormality / defect

MISCARRIAGES, STILLBIRTHS, NEONATAL DEATHS: P-100 MALES, MARRIED EXPERIENCE

Group	Miscarriages + Stillbirths by Trimester				Neonatal Deaths	Live Births	Miscarriages+Stillbirths+Neonatal Deaths / Total Pregnancies	
	1	2	3	Unk			Number	Percent
All males								
Pre-Employment	19+	10*	2	4	4	301	39/336	12
Post-Employment								
No Exposure	1	0	0	0	0	13	1/ 14	7
DNT Exposure	1	0	0	0	0	11	1/ 12	8
TDA Exposure	1	3*	1	0	1	11	6/ 16	38
Multiple Exposure	7*	10	0	0	0	90	17/107	16
Other Exposure	6*	0	1	1+	1	96	9/104	9
TDA-exposed males								
Pre-Employment	2	1	0	0	1	41	4/ 44	9
Post-Employment								
No Exposure	0	0	0	0	0	0	0/ 0	--
DNT Exposure	0	0	0	0	0	3	0/ 3	0
TDA Exposure	1	3*	1	0	1	11	6/ 16	38
Multiple Exposure	3*	0	0	0	0	17	3/ 20	15
Other Exposure	2*	0	0	0	0	14	2/ 16	13

* Includes one miscarriage or stillbirth conceived within nine months of the date of interview.

\+ Includes one tubal pregnancy.

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July 9, 1981

Lloyd B. Tepper, M.D.
Corporate Medical Director
Air Products & Chemicals, Inc.
Box 538
Allentown, PA 18105

Dear Lloyd:

The analysis of fertility at Air Products' Pasadena plant is complete. There is no convincing evidence of a decrease in fertility related to occupational exposure to dinitrotoluene, toluene diamine, or other agents involved in these manufacturing processes.

The study has proceeded according to the method I have presented in recent articles and a letter in the Journal of Occupational Medicine. It is based on information obtained in two rounds of interviews conducted by your staff toward the end of October 1979 and 1980. All dates were provided by the employees at interview, but dates of hire were verified from personnel files. Where the employee's stated date of hire conflicted with that obtained from personnel files, the date from personnel files was used since employee recollection is generally not as accurate. Of 116 employees for whom dates of hire were obtained from plant records, 13 did not agree with stated dates or with information on dates of hire at Air Products' Pensacola plant that had been provided previously. Most discrepancies concerned dates of hire at the Pensacola plant. Dates of job changes came from the employees, but errors in these dates are likely to have minimal effects on exposure-related fertility since most employees did not change jobs and, if they did, it was usually from one exposed job to another, rather than from a job with exposure to one without (or vice versa).

In interviews conducted in 1979 137 employees participated out of 152 listed (90%). In 1980 91 employees were interviewed including 84 who were interviewed for the second time. The results of both rounds of interviews were pooled. Eighteen participants had never been married and thus did not contribute to the analysis. The preponderance (94) of ever-married participants were white males. There were 11 non-white males and 14 females.

Pertinent results are displayed in the table entitled "Married Fertility: AP-180" (attached). This table describes fertility during periods in which employees were married and not permanently separated. Observed and expected births and the resulting ratio or standardized fertility ratio (SFR) are recorded for different slices of group reproductive experience. Pre-employment fertility is set forth in the pair of numerical columns at farthest left. This is followed by two pairs of columns describing the fertility of Pasadena employees during periods of prior work or training at Air Products' Pensacola plant, according to whether or not there was potential risk of exposure to DNT.

The three pairs of columns on the right represent Pasadena plant-related fertility. Since DNT production began in May 1973 and TDA production in April 1976, according to Mr. Pareja, technical manager of the Pasadena plant, persons are assumed to have had no exposure to either chemical prior to May 15, 1973. Reproductive experience related to Pasadena employment before that date, and afterwards, for persons working at jobs with little or no potential for exposure, is recorded in the "No" exposure columns. The second pair of columns describes the reproductive experience related to the period May 15, 1973 through April 14, 1976 during which there was potential for DNT, but not TDA exposure. From April 15, 1976 on there was a possibility for exposure to DNT or TDA; this reproductive experience is summarized in the pair of columns labeled "DNT/TDA".

As I have discussed especially in my recent letter to the editor of the Journal of Occupational Medicine, there is a small artifactual tendency for married fertility after employment to be reduced in comparison with pre-employment fertility (or for no exposure fertility, consisting of the sum of pre-employment and Pensacola and Pasadena "No" exposure experience, to exceed post-employment Pasadena exposed fertility). This is because the U.S. general population from which expected births for the plant population are derived will contain a greater proportion of married women at older ages; and workers are indeed older after employment (exposure) than before. Plant observed fertility, on the other hand, is based only on married years. For example, the weighted average age of the wives of all males in the pre-employment category is 26 (or 27 for the total period of no exposure as defined above). Corresponding weighted average ages for post-employment Pasadena exposure categories range from 31-34, thereby resulting in a six to eight (four to six) percent increase in the proportion married among the general population compared to pre-employment (no exposure) periods. Post-employment Pasadena standardized fertility ratios, therefore, would be expected to be approximately six to eight (four to six) percent lower than corresponding ratios during the period of pre-employment (no exposure).

It was not possible to subdivide the reproductive experience of an individual and assign one portion to one group (e.g. hourly) and another portion to another group (e.g. salaried). Computer capability to do this is being developed. Therefore, only whole individuals could be assigned to groups. Thus on occasion there is duplication between groups: some individuals held both salaried and hourly jobs and were assigned both to salaried and hourly categories; some held both high and low exposure jobs and were assigned to both categories. In order to sum to the correct total, one must subtract the results of the hourly/salaried category from the sum of hourly and salaried; likewise, the high/low exposure results must be subtracted from the sum of high, low, and no exposure groups.

High and low exposure groups represent persons with different sets of job titles, all with potential for exposure, but judged by Mr. Gentile, manager of industrial hygiene for the Chemicals Group, to have more or less potential. Job titles are listed below by potential for exposure:

High Exposure	Low Exposure	No Exposure
control board operator	environ. control technician	clerk
mechanic	instrument technician	buyer
laboratory technician	maintenance foreman	chemist
loader	production day supervisor	accountant
operator	safety engineer	design engineer

- continued on next page -

High Exposure	Low Exposure	No Exposure
operator analyst	safety supervisor	distribution supervisor
quality control technician	shift supervisor	environmental hygienist
welder	loading supervisor	maintenance engineer
		maintenance superintendent
		planner-scheduler
		plant manager
		secretary
		process engineer
		process group leader
		production engineer
		production superintendent
		project engineer
		project group leader
		project manager
		technical manager
		technical superintendent
		warehouseman
		plant hygienist
		purchasing supervisor
		shift supervisor

The categories "mixed exposure", "predominant DNT exposure", "predominant TDA exposure", and "unknown exposure" were derived from information obtained from employees during the 1979 interviews. Employees were asked whether or not they were exposed to DNT or TDA and about the degree to which the chemical was related to their jobs (1=high, 2=medium, 3=low). I have assigned to the mixed exposure group all persons who indicated a potential for exposure to both chemicals except for the following combinations: DNT 1 plus TDA 2/3, which was assigned to DNT; and TDA 1 plus DNT 2/3, which was assigned to TDA. Predominant DNT exposure included the following: DNT 1; DNT 2; DNT 3; DNT; and DNT 1 plus TDA 2/3. Predominant TDA exposure included TDA 1; TDA 2; TDA 3; TDA; and TDA 1 plus DNT 2/3. While this information may be of value in characterizing exposure at the time of interview, its value in assessing exposure over the entire work experience at Pasadena is unknown.

Pre-employment fertility and weighted average ages of wives during that period are similar for hourly and salaried employees, especially when one considers that at a mean age of 27 (vs. 25 for hourly employees) the general population counterparts to salaried employees would contain five percent more married persons. This should increase the pre-employment SFR for salaried employees five percent compared to hourly workers. Since hourly and salaried designations do not appear to affect fertility in and of themselves, there is no difficulty disregarding these categories in relation to fertility.

One will observe that hourly/salaried individuals comprise most of the post-employment experience of salaried persons at Pensacola and Pasadena. Consequently, most of the exposed experience of salaried persons may have been while working at hourly jobs. Thus the contrast of salaried exposed fertility with hourly exposed fertility may have little value. Similarly, since high/low exposed persons comprise most of the exposed experience of the low exposure group, the comparison of post-employment exposed experience of high with low exposure groups is also without merit.

[illegible] Pensacol "No", the [illegible] adena "[illegible] xposure colum[illegible] ttle val e. Fertility [illegible] ure or pre[illegible] yment fertility in all three [illegible] Pensacol exposure "Yes" fertility [illegible] er than expected but the differe[illegible] is not statistically significant. Moreover, the Pensacola "No" exposure fertilit[illegible] is even less. In view of the weakness of the exposure data for Pensacola and the fact that individuals now working at Pasadena who had previously worked at Pensacola represent a [illegible] group of Pensacola employees, I would be hesitant to infer anything about the reproductive effects of Pensacola exposures.

In almost all Pasadena subgroups exposure-related fertility is greater than no exposure or pre-employment fertility. Fertility has surely not been reduced by exposure for these persons. An exception is the category of males with predominant TDA exposure, but the reduction in fertility is not statistically significant. Little meaning can be ascribed to this result. The uncertain value of these exposure designations has already been pointed out. If toluene diamine did in fact reduce fertility at Pasadena, why was this not observed in the high intensity exposure or high duration exposure (seven or more years) groups? Furthermore, the ratio of exposure to no exposure SFRs for those with four or more years of predominant TDA exposure is closer to unity (0.93) than for those with less than four years of such exposure (0.72) - the maximum duration of TDA exposure was 4.5 years.

If duration of exposure is important, as it seemed to be at the OxyChem plant where those with reduced sperm counts averaged 8.0 years of exposure to DBCP, persons at Pasadena with 7.0 or more years of exposure (maximum possible 7.5) should display greater reductions in fertility. These should be most evident during the later period "DNT/TDA", after injury or chemicals have had the opportunity to accumulate. The opposite result, however, is obtained: fertility during the DNT/TDA period is increased in comparison with DNT or no exposure periods.

The statistical calculations are summarized below. The ratio of exposure to no exposure SFRs or the change in fertility with exposure is denoted by θ. When θ exceeds unity, fertility has increased during exposure; where θ is less than unity, fertility has decreased during exposure. The lower bound of the 90% confidence interval indicates the maximum reduction in fertility possible (with 90% confidence) under similar exposure conditions in another group of persons.

Group	p-value	θ	90% C.I. on θ
All males:			
No exposure vs. Pensacola "Yes"	0.19	0.64	(0.28, 1.30)
vs. DNT	0.27	0.53	(0.09, 1.68)
vs. DNT/TDA	0.79	1.17	(0.75, 1.76)
vs. DNT + DNT/TDA	0.64	1.05	(0.69, 1.56)
vs. DNT + DNT/TDA + Pen "Yes"	0.40	0.93	(0.64, 1.32)
Predominant TDA exposed males:			
No exposure vs. DNT/TDA	0.50	0.80	(0.20, 2.32)
vs. DNT + DNT/TDA	0.38	0.68	(0.17, 1.96)
vs. DNT + DNT/TDA + Pen "Yes"	0.33	0.63	(0.16, 1.82)

In summary, I feel it is reasonable and proper to conclude that there has been no effect of occupational exposures at the Pasadena plant on group fertility.

Please let me know if you would like additional information or explanation.

With many thanks for your generous assistance,

Yours truly,

Richard J. Levine

Richard J. Levine, M.D.
Chief of Epidemiology

cc: Dr. James E. Gibson, Director of Research

MARRIED FERTILITY; AP-180

Group	Pre-Employment		Post-Employment									
			Pensacola Exposure				Pasadena Exposure					
			No		Yes		No		DNT		DNT/TDA	
	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR	O/E	SFR
All employees	147/75.2	1.95	1/1.4	0.74	6/4.9	1.22	2/1.8	1.09	2/2.0	0.99	20/9.1	2.21
All males	123/63.3	1.94	1/1.4	0.74	6/4.9	1.22	2/1.6	1 29	2/2.0	0.99	20/9.0	2.22
White	115/60.1	1.91	1/1.4	0.74	6/4.9	1.22	2/1.5	1.33	2/1.6	1.24	17/8.0	2.14
Non-white	8/ 3.2	2.52	-----	----	-----	----	0/0.1	0.00	0/0.4	0.00	3/1.1	2.82
Spanish surname	9/4.0	2.24	-----	----	-----	----	0/0.1	0.00	-----	----	2/0.8	2.42
Hourly	78/41.7	1.87	1/1.0	1.01	6/4.2	1.43	0/0.2	0.00	2/2.0	0.99	20/9.0	2.23
Salaried	57/29.2	1.95	1/1.4	0.74	4/3.7	1.07	2/1.4	1.42	0/0.6	0.00	1/0.8	1.30
Hourly/salaried	12/ 7.6	1.58	1/1.0	1.01	4/3.0	1.32	0/0.0	0.00	0/0.6	0.00	1/0.7	1.36
High exposure	74/39.3	1.88	1/1.0	1.01	6/4.2	1.43	0/0.1	0.00	2/2.0	0.99	19/8.9	2.13
Low exposure	38/18.2	1.65	1/1.3	0.77	4/3.7	1.07	0/0.1	0.00	0/0.6	0.00	3/1.2	2.43
High/low exposure	13/ 8.1	1.61	1/1.0	1.01	4/3.0	1.32	0/0.0	0.00	0/0.6	0.00	2/1.1	1.78
No exposure	32/13.8	2.31	0/0.1	0.00	-----	----	2/1.4	1.40	-----	----	------	----
Mixed exposure	48/25.9	1.85	1/1.0	1.04	6/4.5	1.33	0/0.1	0.00	1/1.0	1.00	8/3.6	2.22
Predominant DNT exp.	19/10.2	1.86	0/0.0	0.00	0/0.0	0.00	0/0.0	0.00	1/0.4	2.50	7/2.8	2.50
Predominant TDA exp.	20/11.4	1.75	0/0.3	0.00	0/0.2	0.00	0/0.0	0.00	0/0.4	0.00	3/2.2	1.36
Unknown exposure	4/ 2.0	1.96	-----	----	0/0.2	0.00	-----	----	0/0.2	0.00	2/0.5	4.18
No exposure	32/13.8	2.31	0/0.1	0.00	-----	----	2/1.4	1.40	-----	----	------	----
⩾ 7.0 years exposure	26/14.8	1.76	1/1.0	1.04	4/3.3	1.21	0/0.1	0.00	1/1.5	0.68	5/1.5	3.25
Pensacola exposed	17/ 8.9	1.92	1/1.0	1.01	6/4.9	1.22	0/0.0	0.00	0/0.2	0.00	0/0.1	0.00
All females*	24/11.9	2.01	-----	----	-----	----	0/0.3	0.00	-----	----	0/0.0	0.00

O/E - observed/expected births; SFR - standardized fertility ratio; DNT: May 1973 through April 1976, the period during which only dinitrotoluene was produced; DNT/TDA: April 1976 and thereafter, when both dinitrotoluene and toluene diamine were manufactured

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All females were hourly employees; one had worked at both hourly and salaried jobs. One female was non-white.

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March 16, 1982

Lloyd B. Tepper, M.D.
Corporate Medical Director
Air Products & Chemicals Inc.
Box 538
Allentown, PA 18105

Dear Lloyd:

I am sorry you didn't have a chance to drop by the lab the day of CIIT's annual meeting. I have enclosed copies of the slides relating to Air Product's Pasadena plant, which I used in my talk on the reproductive experience of workers exposed to dinitrotoluene and toluene diamine at CIIT's recent conference on the toxicity of nitroaromatic compounds.

Data for the slides entitled "DNT: Plant A" and "TDA: Plant A" comes from the table "Married Fertility: AP-180" in my letter to you of July 9, 1981. This table is based on information obtained in two rounds of interviews conducted by your staff with employees of your Pasadena plant during October 1979 and 1980. "Pre-Employment + Non-exposed" on the slide is the sum of Pre-Employment, Pensacola No Exposure, and Pasadena No Exposure from the table. Exposed for the DNT slide is the sum of Pasadena DNT and DNT/TDA exposure from the table; exposed for the TDA slide is merely DNT/TDA exposure in the table. High intensity and low intensity in the slides corresponds to high and low exposure in the table.

Data for the slides entitled "Abnormalities or Defects in Liveborn Offspring: Plant A" and "Miscarriages, Stillbirths, Neonatal Deaths: Plant A" was obtained from those employees of the Pasadena plant who had been interviewed during October 1979 and/or 1980 and who were interviewed again in October 1981. Information on abnormalities or defects and miscarriages, stillbirths, and neonatal deaths for reproductive events which occurred prior to the previous round of interviews was gathered in October 1981 and presented in the slides. It is evident that there has been no increase in these adverse reproductive outcomes associated with DNT or TDA exposure at the plant.

An increased frequency of miscarriages, stillbirths, and neonatal deaths was found to be associated with TDA exposure in a study I performed at a TDI manufacturing plant. The risk of these adverse reproductive events, however, did not appear to be related to duration or intensity of exposure; moreover, the increased risk disappeared once TDA exposure had ceased i.e. when exposed individuals were transferred to another part of the plant. For these reasons, with a p-value of 0.03, I am not prone to make much of the association, which might have been due to chance alone, especially in view of the fact that this observation was not corroborated by data from two other plants I have studied. Data from a third plant is being analyzed now.

I hope this information is of some assistance to you. We plan to finish the fertility analysis at Pasadena incorporating data from the recent interviews once we have received clarification of some questions we asked Mr. Eldridge.

Yours truly,

Richard J. Levine

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Chief of Epidemiology

cc: Dr. Robert A. Neal
Dr. Ernest Blade

DNT: PLANT A

GROUP	PRE-EMPLOYMENT + NON-EXPOSED SFR	(O/E)	EXPOSED SFR	(O/E)
All Males	1.90	(126/66.3)	2.00	(22/11.0)
High Intensity			1.93	(21/10.9)
Low Intensity			1.67	(3/ 1.8)
>7 years exposure			2.00	(6/3.0)
<7 years exposure			2.00	(16/8.0)

TDA: PLANT A

	Pre-employment + Non-exposed		Exposed	
	SFR	(O/E)	SFR	(O/E)
All males	1.90	(126/66.3)	2.22	(26/9.0)
High intensity			2.13	(19/8.9)
Low intensity			2.43	(3/1.2)
>7 years exposure			3.25	(5/1.5)
<7 years exposure			2.00	(15/7.5)

ABNORMALITIES OR DEFECTS IN LIVEBORN OFFSPRING: PLANT A

GROUP	NUMBER WITH ABNORMALITIES/DEFECTS / LIVE BIRTHS	
	NUMBER	PERCENT
All Males		
Pre-employment	4/81	5
Post-employment	2/18	11
No exposure	1/2	50
DNT exposure	0/2	0
DNT/TDA exposure	1/14	7

MISCARRIAGES, STILLBIRTHS, NEONATAL DEATHS: PLANT A

GROUP	Miscarriages-Stillbirths-Neonatal Deaths / Reported Pregnancies NUMBER	PERCENT
All Males		
Pre-employment	12/89	13
Post-employment	3/21	14
No exposure	1/3	33
DNT exposure	0/2	0
DNT/TDA exposure	2/16	15