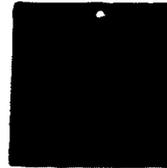


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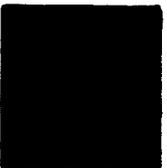
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HEALTH STUDY

FINAL REPORT

EXECUTIVE SUMMARY



University of Massachusetts  
Division of Public Health



February 16, 1987

84-870000079  
FYI-OTS-0387-0528

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## INTRODUCTION

This report presents the results of a health study of employees of the D.E.C. Hudson L.S.I. facility conducted by the University of Massachusetts School of Public Health (E. Calabrese and H. Pastides, Co-Principal Investigators). This summary presents, in abbreviated form, the major study findings. A comprehensive report including further background information, methodologic details and complete results follows this summary. All tables presented in this summary are also found in the complete report.

This investigation was initiated by management in response to concern raised by two employees about the possibility of an elevated risk for spontaneous abortion among manufacturing employees. While this adverse health outcome was the study's main focus, a wide variety of reproductive outcomes as well as the prevalence of general health measures were examined.

All current employees at the time of the study, as well as all former L.S.I. Hudson manufacturing workers (not terminated for cause) were eligible for study. During two phases of interviewing, useable data were collected from a total of 744 employees. Spouses of currently married male employees were interviewed by telephone to identify their history of pregnancy outcomes.

Three groups of employees were compared with respect to the occurrence of reported health outcomes: Photo employees refer to manufacturing and other workers exposed to a wide array of chemicals including glycol ethers used in a photosensitive process of semiconductor manufacture. Diffusion employees refer to manufacturing and other workers exposed to chemicals not including glycol ethers and involving other activities in semiconductor manufacture. Non-exposed employees refer to workers with a wide variety of occupational responsibilities at the Hudson facility exclusive of jobs involving chemical exposures. This group included clerical staff, engineers, administrative employees, and others.

### Reproductive Outcomes

For the purposes of this report "abortion" refers to induced abortions reported by respondents; "miscarriage" refers to reported spontaneous abortions prior to 29 weeks of gestation; and "stillbirth" refers to spontaneous abortions after 28 weeks of gestation or a fetus pronounced dead at time of birth. For workers in the Photo and Diffusion groups, only pregnancies occurring after date of first employment at Hudson were considered in the following presentation of results since prior pregnancy outcomes could not be attributable to Hudson occupational exposures. For the Non-exposed group, however, all pregnancies were considered. This was done to enhance the precision with which quantitative comparisons could be made.

Table 1 presents the reported pregnancy outcomes in the three groups. The miscarriage ratio among females in the Diffusion group, defined as the proportion of total pregnancies resulting in a miscarriage, was found to be slightly more than twice the rate found among Non-exposed females (38.9% vs. 17.8%). This translates into a Relative Risk of 2.18 (the ratio of Diffusion miscarriages to Non-exposed miscarriages); this risk was significantly greater than a difference likely to have been due to chance alone. The miscarriage rate among Photo females was found to be 31.3%, translating to a Relative Risk of 1.75 when compared to the Non-exposed females. This ratio, while elevated, was not found to be significantly different in a statistical sense from the miscarriage ratio in the Non-exposed females.

TABLE 1

PREGNANCY OUTCOME AMONG FEMALE EMPLOYEES BY EXPOSURE GROUP

EXPOSURE GROUP	ABORTIONS		STILLBIRTHS		MISCARRIAGES		LIVEBIRTHS	
	N	RATIO	N	RATIO	N	RATIO	N	RATIO
PHOTO	2	(12.5)	0	(0.0)	5	(31.3)	9	(56.3)
DIFFUSION	1	(5.6)	0	(0.0)	7	(38.9)	10	(55.6)
NONEXPOSED	35	(8.8)	2	(0.5)	71	(17.8)	290	(72.9)

Ratio expressed as a number of events per 100 pregnancies.

Relative risk of miscarriage comparing Photo to Nonexposed women = 1.75; 95% CIE = (0.82, 3.73).

Relative risk of miscarriage comparing Diffusion to Nonexposed women = 2.18; 95% CIE = (1.18, 4.04).

Relative risk of miscarriage comparing combined exposure groups (Photo + Diffusion) to Nonexposed women = 1.98; 95% CIE = (1.20, 3.27).

Miscarriages in the Diffusion group females were reported to occur at an earlier time, on average, than those in females in the Photo and Non-exposed groups (6.3 weeks vs. 10.2 and 11.6 weeks, respectively). These results are reported in Table 2.

TABLE 2  
DISTRIBUTION OF GESTATIONAL AGE (WEEKS) FOR MISCARRIAGES  
OCCURRING AMONG FEMALE DEC EMPLOYEES

PARAMETER	PHOTO	DIFFUSION	NONEXPOSED	ANOVA
MEAN	10.2	6.3	11.6	F = 2.630
STD. DEV.	2.49	1.38	6.31	p = 0.079
95% CIE	( 7.1, 13.3)	( 5.0, 7.6)	(10.1, 13.1)	
RANGE	6.0, 12.0	4.0, 18.0	1.0, 28.0	
MEDIAN	11.0	6.3	11.5	
NUMBER	5	7	71	

In order to determine whether the reported differences in miscarriage ratios could be attributed to any other factors potentially related to the risk of miscarriage and to exposure group, multivariate statistical procedures were employed. Factors which were taken into account through multiple logistic regression analysis included: age at pregnancy, number of previous pregnancies, presence of prior induced abortions, smoking during pregnancy, alcohol consumption during pregnancy, caffeine consumption during pregnancy, and others. No substantial deviations from the relative risks reported above were identified in these analyses. In no case did the risk of miscarriage among Diffusion females become lower than that reported in Table 1; in multivariate analyses the risk was in the range of 2.8 to 3.4.

Similarly, in no analysis did the risk for Photo females become lower than that reported in Table 1; the risk of miscarriage ranged from 2.3 to 2.9.

To explore whether the relative risk identified could have been due to differences in miscarriage risk present prior to Hudson employment, pregnancy outcomes before first Hudson employment were compared. As seen in Table 3, no meaningful differences in risk were identified; miscarriage rates in all three groups were based on small numbers and were between 12.5% and 16.8%.

With respect to other reproductive outcomes, no differences were identified in the reported occurrence of congenital anomalies, mean birth weight of live births, infertility, or spotting or bleeding during pregnancy (apart from miscarriage).

When pregnancy outcomes of spouses of male Hudson employees were compared, no significant differences in the ratios of reported miscarriage were identified (Table 4). The ratios were between 5.3% and 12.5%; given the relatively small numbers of

events, these differences could have been attributable to chance, but conclusions about risk must be cautious.

TABLE 3

PREGNANCIES OCCURRING PRIOR TO DEC EMPLOYMENT AMONG FEMALE EMPLOYEES

EXPOSURE GROUP	ABORTIONS		STILLBIRTHS		MISCARRIAGES		LIVEBIRTHS	
	N	RATIO	N	RATIO	N	RATIO	N	RATIO
PHOTO	4	(50.0)	0	(0.0)	1	(12.5)	3	(37.5)
DIFFUSION	3	(50.0)	0	(0.0)	1	(16.7)	2	(33.3)
NONEXPOSED	30	(8.5)	2	(0.6)	59	(16.8)	261	(74.1)

Ratio expressed as a number of events per 100 pregnancies.

Relative risk of miscarriage comparing Photo to Nonexposed women = 0.75; 95% CIE = (0.12, 4.73).

Relative risk of miscarriage comparing Diffusion to Nonexposed women = 0.99; 95% CIE = (0.16, 6.04).

Relative risk of miscarriage comparing combined exposure groups (Photo + Diffusion) to Nonexposed women = 0.85; 95% CIE = (0.23, 3.14).

TABLE 4

PREGNANCY OUTCOME AMONG SPOUSES OF MALE EMPLOYEES, BY EXPOSURE GROUP

EXPOSURE GROUP	ABORTIONS		STILLBIRTHS		MISCARRIAGES		LIVEBIRTHS	
	N	RATIO	N	RATIO	N	RATIO	N	RATIO
PHOTO	0	(0.0)	0	(0.0)	2	(12.5)	14	(87.5)
DIFFUSION	0	(0.0)	0	(0.0)	1	(7.7)	12	(92.3)
NONEXPOSED	1	(5.3)	0	(0.0)	1	(5.3)	17	(89.5)

Ratios expressed as a number of events per 100 pregnancies.

Relative risk of miscarriage comparing Photo to Nonexposed women = 2.38; 95% CIE = (0.24, 23.84).

Relative risk of miscarriage comparing Diffusion to Nonexposed women = 1.46; 95% CIE = (0.10, 21.33).

Relative risk of miscarriage comparing combined exposure groups (Photo + Diffusion) to Nonexposed women = 1.97; 95% CIE = (0.22, 17.53).

General Health Outcomes

The examination of differences in the prevalence of reported symptoms and illnesses between Photo, Diffusion, and Non-Exposed groups for males and females was conducted to identify general associations with occupational group; symptoms occurring any time during the most recent five years (the approximate history of the Hudson facility) were inquired about first. Table 5 presents a summary of the significant associations found. When compared to females in the Non-exposed group, females in the Photo group were more likely to report frequent or severe nausea, sore throats or rash, arthritis and diabetes. Females in the Diffusion group were significantly more likely than their Non-exposed counterparts to report frequent or severe sore throats or headaches and significantly less likely to report back problems other than slipped disk. Males in the Diffusion group were more likely than Non-exposed males to report frequent or severe nausea. Some of the associations were based on small numbers of persons reporting the symptom or illness and should not be taken as indicative of risk. This was most notable for reporting of diabetes.

TABLE 5  
SUMMARY TABLE FOR SYMPTOMS SIGNIFICANTLY ASSOCIATED \*  
WITH EXPOSURE, BY SEX GROUP

EXPOSURE GROUP	REPORTED SYMPTOM	REPORTING SYMPTOMS				PREVALENCE RATIO	95% CIE (LL, UL)
		EXPOSED N	EXPOSED %	NONEXPOSED N	NONEXPOSED %		
<b>FEMALES</b>							
DIFFUSION	HEADACHE	31	47.0	73	21.7	2.16	1.56, 3.00
DIFFUSION	OTHER BACK PROBLEMS	6	9.1	72	21.4	0.42	0.19, 0.94
DIFFUSION	SORE THROAT	8	11.9	13	3.9	3.07	1.32, 7.11
PHOTO	ARTHRITIS	10	15.9	23	6.8	2.32	1.16, 4.63
PHOTO	DIABETES**	3	4.5	2	0.6	7.55	1.29, 44.29
PHOTO	NAUSEA	7	10.6	12	3.6	2.94	1.20, 7.20
PHOTO	RASH	9	13.4	19	5.7	2.38	1.12, 5.02
PHOTO	SORE THROAT	7	10.6	13	3.9	2.73	1.13, 6.57
<b>MALES</b>							
DIFFUSION	NAUSEA	7	7.9	1	0.9	8.73	1.09, 69.65

\* A symptom with a prevalence ratio whose confidence interval estimate does not include 1.0.

\*\* Numbers too small to be reliable.

In a second analysis, the temporal relationship between employment at Hudson and first occurrence of the symptoms or illness was examined. While etiologic inference is not much stronger based on this analysis, it does indicate that some of the associations of the previous analysis included symptoms whose first onset preceded employment at Hudson. Table 6 depicts the associations between occupational group and symptoms whose onsets were not identified as preceding Hudson employment. Since incidence is difficult to study due to the periodic or recurrent nature of some of these symptoms, etiologic inferences should be guarded.

TABLE 6  
SUMMARY TABLE FOR SYMPTOMS SIGNIFICANTLY ASSOCIATED TEMPORALLY  
WITH EXPOSURE, BY SEX GROUP\*

EXPOSURE GROUP	REPORTED SYMPTOM	REPORTING SYMPTOMS				PREVALENCE RATIO	95% CIE (LL, UL)
		EXPOSED		NONEXPOSED			
		N	%	N	%		
<b>FEMALES</b>							
DIFFUSION	HEADACHE	31	47.0	73	21.7	2.16	1.56, 3.00
PHOTO	ARTHRITIS	5	7.9	7	2.1	3.81	1.25, 11.63
PHOTO	NAUSEA	7	10.6	12	3.6	2.94	1.20, 7.20
PHOTO	RASH	9	13.4	19	5.7	2.38	1.12, 5.02
PHOTO	SORE THROAT	6	9.1	11	3.3	2.76	1.06, 7.20
<b>MALES</b>							
DIFFUSION	NAUSEA	7	7.9	1	0.9	8.73	1.09, 69.65

\* A symptom with a prevalence ratio whose confidence interval estimate does not include 1.0.

## Discussion

The finding of a significantly increased risk of miscarriage among female Diffusion employees, and a non-significantly higher risk among female Photo employees, at the DEC Hudson facility when compared to an internal Non-exposed group needs to be considered in light of general medical knowledge about this reproductive outcome and also in light of the limitations of the present study.

The data reported here indicate a positive association between occupation in the Diffusion area and risk for spontaneous abortion among females, beyond that which would be expected by chance. The observed rate of miscarriage of this group was higher than in the comparison group and also higher than the level observed among these women prior to employment at the Hudson facility. This relation persisted even after controlling for a variety of risk factors for which data were available. Certainly, this finding was not related to the original study hypothesis concerning risks associated with glycol ether exposures. Nevertheless, it would be imprudent to neglect it based on this lack of hypothesis. The elevated risk among females in the Photo group, while not statistically significant, corresponds to a 31.3% occurrence of spontaneous abortion; this is higher than that observed in most population surveys.

The relatively small number of pregnancies used as the basis for calculating the miscarriage ratio in both exposure groups should be borne in mind. This was a function of the number of production workers employed and also of the relatively short history of the facility. Specifically, the miscarriage ratios were based on only 34 pregnancies in both manufacturing groups. Regardless of the levels of statistical significance, ratios based on small numbers of events are more likely to change substantively when further observations are included; this underscores the need to replicate and extend these results.

Retrospective surveys of past pregnancies have contributed the largest amount of information known about population rates of spontaneous abortion. The miscarriage ratio (total number of miscarriages divided by total number of pregnancies) is the usual index used to examine population risk (1). General population surveys, as well as specific research studies, have generally found miscarriage ratios in the 10-20% range (5-21). The completeness of such research depends on the willingness and ability of respondents to report past events of this type. Reasons for underreporting could include: fear that it might be thought of as having been elective; lack of knowledge that such an event occurred, especially if very early in pregnancy; and incomplete recall. Reasons for overreporting can include a perceived health threat resulting from an occupational exposure, desire to somehow damage management or corporate image, and others. Recall bias is not believed to be a prime explanation

for the findings of this study; a detailed discussion of this issue is included in the report.

The fact that women who continue working are sometimes at higher risk for miscarriage than those who terminate employment (to care for the infant) has been identified by Axelsson (22). This study attempted to address this issue by identifying former employees, not terminated for cause, and collecting information on health outcomes by telephone interview. The number of such employees was small, however, and did not affect the results.

Known and purported causes of miscarriage include malformation, chromosomal abnormalities, gynecologic pathology, immunological factors, progesterone deficiency, infectious disease, IUD use, smoking and alcohol during pregnancy, maternal age and birth order, and chemicals and other environmental exposures. While this study collected and analyzed information on many of these risk factors in light of occupational group, it would be impossible to completely examine all possible risks in detail. The attribution of the observed increased risk in this study cannot, therefore, be causally linked with occupation. The inherent weakness of working with self-reported data from human populations often precludes a "proven" or "cause and effect" appraisal.

Studies to date have identified the testicular toxicity of acute glycol ether exposure in mice, rats, and rabbits (27-34). Observed toxic effects include atrophy in size and weight of testes, and degeneration of germinal epithelium. Reversible fertility loss has also been identified in these male species (30,35), as has teratogenicity (36-39). The nature and severity of events has varied depending on dose and route of administration. The fact that animal experiments indicate that a biological effect of glycol ether was to cause spontaneous abortion through its action on male gametes should not be viewed as an argument against a potential effect on the human female, since sufficient studies of females have not been conducted.

Finally, one needs in the future to better account for actual exposure levels encountered in the Hudson occupational setting. Only with better monitoring will detailed exposure information be valuable enough to include in an analysis of the data. With respect to glycol ethers, for example, previous Hudson Industrial hygiene monitoring data indicated very low or non-discernable exposure levels among persons in the Photo area. Again, this should not be used to discount the present association, but should, instead, underscore the need to conduct more complete monitoring. Furthermore, the present study had to rely on respondent information to help categorize historical occupational exposure since company employment records were not adequate for this purpose. The results of this study should bear replication and validation in future investigations, using comparably exposed groups of workers.

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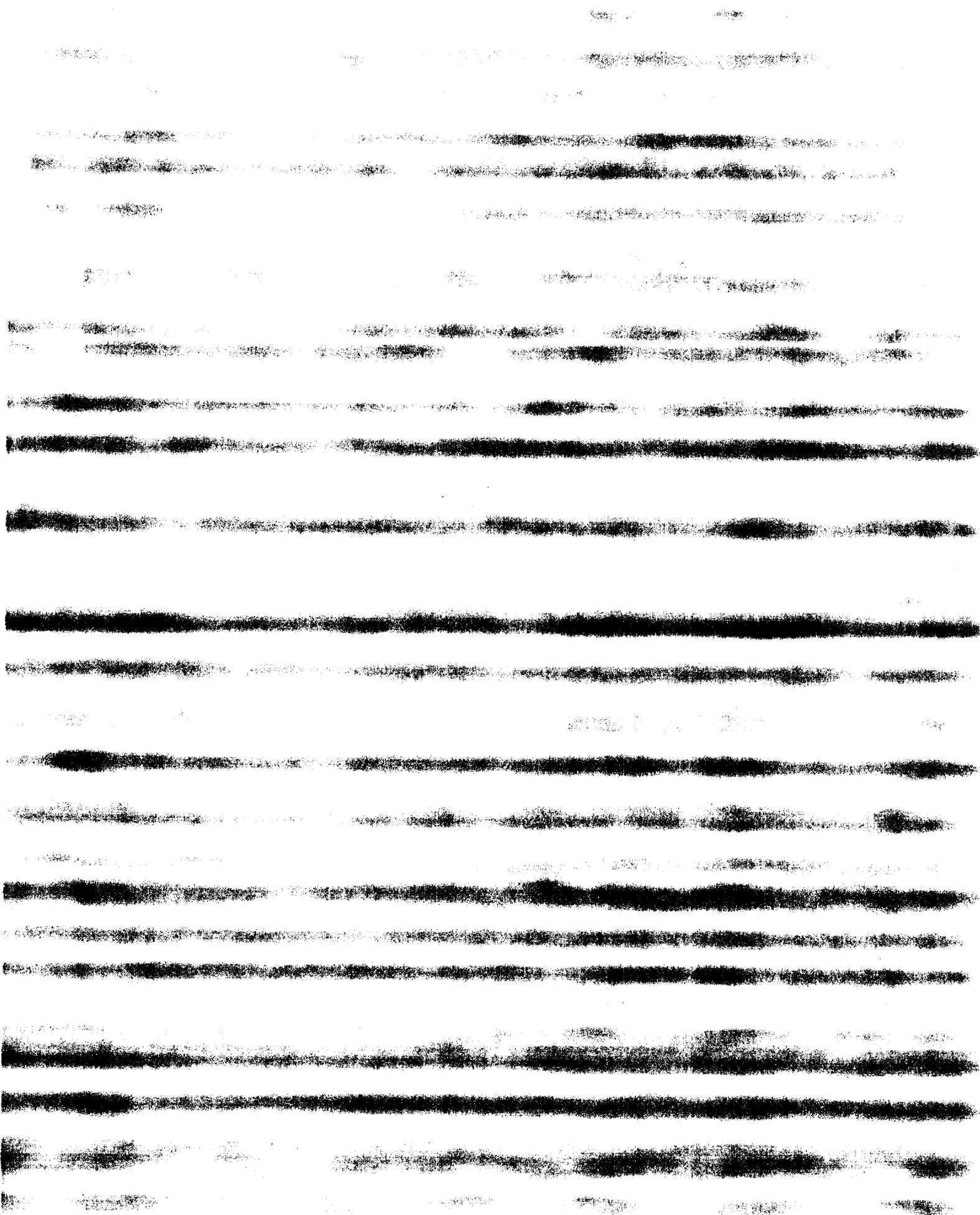
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DIGITAL EQUIPMENT CORPORATION

HEALTH STUDY

FINAL REPORT

University of Massachusetts  
Division of Public Health

February 16, 1987

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## INTRODUCTION

This report presents the results of a study conducted by researchers at the University of Massachusetts School of Health Sciences, Division of Public Health, under a contract from the Digital Equipment Corporation (DEC).

This study was conducted to evaluate specific health experiences of employees working in manufacturing positions which involve exposure to certain chemicals at the DEC Hudson facility. The investigation was initiated by management in response to concern raised by two employees about the possibility of elevated risk for spontaneous abortion among manufacturing employees working in the photolithographic area of semiconductor manufacturing.

The primary health outcome of interest was a person's reproductive history in relationship to employment in manufacturing at the Hudson facility. This included any adverse outcome of pregnancy as well as reported infertility, birth weight, and pre-term delivery. A secondary outcome of interest was to determine the prevalence of various symptoms and illnesses as related to workplace exposure. The following general health outcomes were considered: occurrence within the past five years of arthritis, slipped disk, other back problems, diabetes, high blood pressure, cancer, thyroid problems, gallbladder problems, respiratory problems, kidney problems, seizure disorders, and anemia; and the reporting of frequent or severe sore throats, headaches, dizziness, nausea, rash, and eye strain.

Both for reproductive and general health prevalence outcomes, the study was intended to gather valid observational data so that management could better determine whether health problems in relation to work exposures were indicated and, if so, to later examine potential causes and mechanisms which could eventually lead to protective intervention.

## METHODS

It was expected that the total number of pregnancies experienced by manufacturing workers since the opening of the Hudson facility would be small. A total sample of current manufacturing workers was, therefore, recruited. Additionally, a list of all former manufacturing workers from this facility was requested. Current non-manufacturing workers with previous fab exposure were identified and recruited, as was a small number of former fab employees no longer working for DEC. Former employees were not contacted if they had been terminated "for cause"; the remainder had information collected by telephone interview.

In addition to the photolithographic group, two comparison groups of workers employed in the same facility were also

selected for participation. The first was a group of employees involved in aspects of semiconductor production where Photo-resist chemicals were not in use. These workers were employed in the diffusion area, ion implant, and epitaxi. These workers were all exposed to a variety of solvents, acids and metals, but had little usual exposure to glycol ethers and related chemicals. The second comparison group was composed of workers not exposed to industrial chemicals at Hudson and included clerical and administrative staff, engineers, and other employees not involved in semiconductor production. Using a company supplied computer list, a random sample of non-exposed workers was selected on a group matched basis to approximate the age and sex distribution of the workers in the photolithographic group. Data were collected during two phases: November and December of 1984, and April and May 1986. The second phase was initiated since the number of pregnancies occurring after employment in this facility among females in the non-exposed group was too small to derive a stable estimate of the miscarriage ratio to be used as a comparison. This was likely caused as a result of the lower mean duration of employment at the facility within this group. For the same reason, it was decided to include pregnancies occurring prior to employment in this facility for this group. Before the second phase of study, a small number of production workers not previously included on the personnel list were identified by management; they were also invited to participate. After the first phase workers were notified that additional interviews were needed to conclude the study. Included in the final study analyses were: 67 female and 69 male, photolithographic employees; 67 female and 91 male, non-photolithographic, manufacturing employees; and 337 female and 113 male non-exposed employees. The term "Diffusion Worker" is used in this report to denote production workers who were classified as not having routine exposures to the photo-resist chemicals used in photolithography. They included primarily diffusion operators, but also workers in ion implant and epitaxi. The participation rate was 85% overall and did not differ significantly by exposure status, sex, or study phase.

Potential participants were informed of a "general health surveillance" effort being conducted by the University and invited to participate in a personal interview with trained female interviewers during work hours. The interviewers, who had no relatives or friends working at the facility, were carefully trained and were kept blind to specific hypotheses of interest. Interviews were conducted in private rooms at the facility at scheduled times.

After receiving signed, informed consent, interviewers used company maps of room layouts and work stations to elicit complete work histories of all participants. Final classification of photolithographic or non-photolithographic status was made on the basis of detailed occupational history information collected during the personal interview; this classification was not made by the interviewers. For each position held at the facility, respondents were asked to report the work stations where they

were occupied, including the approximate proportion of their work day at each station identified. Maps of the work stations were used as aids for the respondents during the interview. A chemical list was also shown to production workers to help identify products generally used by the respondents. Final determination as to exposure to photolithographic chemicals was made by the investigators.

Workers' exposure and health outcome histories were also included in the current analysis if they were working as a DEC fab worker during the period immediately preceding the opening of the Hudson facility. During this period, the fab process was conducted at a site leased by DEC. The fabrication processes, including materials used, were the same as those found at the Hudson location. As used in this report, the term "Hudson facility" will refer to this exposure as well.

In addition to cost centers, job titles, work stations, and chemicals used, employees provided information about their safety practices including the habit of wearing gloves and respirators if recommended or required, and their involvement in cleaning up chemical spills.

Other information collected through the standardized, structured questionnaire included sociodemographic characteristics; prior health history; current health status including various symptoms of illness; contraceptive and menstrual histories of female participants; complete reproductive experience; current and past use of alcohol, tobacco, and prescription medications; and participation in hobbies involving significant exposures to solvents and other chemicals. The reproductive history included questions about: infertility; use of prenatal care; complications during pregnancy; pregnancy outcomes including induced abortion, miscarriage, and stillbirth; malformations among live births; birth weight; pre-term delivery; and use of tobacco, alcohol, and caffeine containing products during each pregnancy.

When relevant information about pregnancy outcome could not be recalled by respondents, permission was sought to contact physicians or hospitals in order to obtain this data. Uncertain information which could not be verified in this way was coded as missing. The decision not to follow-up all reported pregnancy information with attempts to document the event through medical records, but to follow-up only when information was reported as "uncertain" or "don't know", was based on several factors. Firstly, there was no central company health record or other uniform source for accessing such information accurately and consistently for all respondents. The only alternative was, therefore, to rely on communication with community physicians and hospitals to access such documentation. Such cooperation was likely to be only partially successful. Furthermore, there is a known under-reporting of potential miscarriages, especially those occurring early, to health care providers.(1) Finally, the group under study was generally well educated, therefore representing

women less likely to be unaware, and less likely to forget significant life events such as miscarriages. Also important to consider was the likelihood of over-reporting of adverse events by a group perceived to be threatened by exposure. While two employees had expressed a concern to company officials, it was clear that there was no generalized or vocal employee concern about potential problems at the time of data collection for this study. A discussion of the likelihood of recall bias in this study is included in this report.

Currently married male participants were asked permission to have their spouses contacted for participation in a structured telephone interview to elicit their complete reproductive experience. Of the 127 married male respondents, 121 (95%) spouse interviews were successfully completed.

#### METHODS OF ANALYSIS

The Relative Risk (RR) was used as the measure of association between exposure and reproductive health outcome in this study. For general health symptoms, the prevalence ratio was calculated. The relative risk provides a comparison of the occurrence of a health outcome in an exposed group and in a referent group. The interpretation of a relative risk greater than 1.0 is that the group with the exposure of interest is considered to be at an increased risk of developing the associated condition in comparison to the group not having this exposure. The relative increase in risk is given by the magnitude of the relative risk, so that a group exposed to some particular factor with a relative risk of 2.0 has a risk of disease that is approximately twice that of a non-exposed group. A relative risk of 1.0 indicates that there is no increase or decrease in risk associated with the exposure. Relative risks less than 1.0 are indicative of exposures that are associated with a reduction in risk for a particular condition. A relative risk is considered to differ significantly from unity if the 95% confidence interval estimate (CIE) constructed about the point estimate of this risk measure does not include the value of 1.0 (e.g. RR = 3.0; 95% CIE = 1.5, 5.0 or RR = 0.6; 95% CIE = 0.2, 0.9).

The upper and lower limits of the confidence intervals for the relative risk were obtained by exponentiating the endpoints of the confidence interval for  $\ln(\text{RR})$ . The variance estimate for  $\ln(\text{RR})$  was derived using the delta-method, first order Taylor series expansion.

A hypothetical example is presented below. In this example, the significantly elevated relative risk is noted with an asterisk.

RELATIVE RISK (RR) AND 95% CONFIDENCE INTERVAL ESTIMATE (CIE) FOR  
HYPOTHETICAL DATA

	TOTAL WITH SYMPTOMS		TOTAL WITHOUT SYMPTOMS		RR	95% CIE (LL, UL)	CHI SQUARE
	N	%	N	%			
GROUP 1	19	28.4	48	71.6	1.31	(0.85, 2.01)	1.39
GROUP 2	31	47.0	35	53.0	2.16*	(1.56, 3.00)	18.33
NONEXPOSED	73	21.7	263	78.3	--		

\* Indicates significantly elevated relative risk.

In the example, a comparison of individuals in hypothetical GROUP 2 to the Non-exposed group produced a significantly increased relative risk while comparing GROUP 1 to those Non-exposed yielded a relative risk which did not differ significantly from one. In the presence of a relative risk and its confidence interval, the examination of a chi-square statistic does not offer any additional useful information.

For multivariate analyses of exposures, health outcomes, and control variables, multiple logistic regression was performed, utilizing the BMDPLR program. Odds ratios and 95% CIE's were calculated from the estimated regression coefficients and standard errors provided in these analyses. Endpoints for confidence intervals for the coefficients were exponentiated to obtain the limits for the odds ratio.

In the reproductive analyses, every pregnancy for each woman was considered separately. For example, a woman having three pregnancies could contribute two livebirths and one miscarriage to the investigation. Pregnancies which occurred for women in the Non-exposed group prior to employment at the Hudson facility were included along with those occurring after DEC employment. This analysis resulted in a comparison more closely matched on age at time of pregnancy, a variable known to be associated with the occurrence of miscarriages, and yielded a larger sample for increasing the power of the study to detect a difference if one did indeed exist. Analyses examining the potential of a differential recall for exposed and non-exposed individuals were also conducted and are presented in the discussion section.

The analysis of the reproductive data began with examination of a wide range of demographic variables and potential confounding factors by exposure grouping. Miscarriage ratios were then calculated by group, followed by additional univariate analyses of related variables (e.g. gravidity). Multiple

logistic regression analyses were then performed to obtain exposure odds ratios adjusted for potential confounders.

Analyses of data obtained from male and female employees were conducted separately. As will be noted later, the number of pregnancies contributed by spouses of male workers to this investigation was relatively small and multivariate analyses were, therefore, not pursued with these pregnancies.

## RESULTS

### Study Population

In the first phase of data collection, 460 subjects were invited to participate and 438 (95.2%) were entered into the study. In the second phase, an additional 414 were invited and 306 (74.0%) participated, for a total of 744 subjects. The number entered and studied by phase, exposure group and sex is shown in Table 1.

TABLE 1

SUBJECTS ENTERED INTO THE STUDY AND INCLUDED IN THE ANALYSIS

PHASE	GROUP	MALE	FEMALE	TOTAL
I	PHOTO	62	47	109
	DIFFUSION	90	55	145
	NONEXPOSED	109	75	184
II	PHOTO	7	20	27
	DIFFUSION	1	12	13
	NONEXPOSED	4	262	266
TOTAL		273	471	744

### Reproductive Outcomes: Females

For the purpose of this report "abortion" refers to an induced abortion reported by a respondent; "miscarriage" refers to a reported spontaneous abortion prior to 28 weeks gestation; and "stillbirth" refers to a spontaneous abortion after 29 weeks of gestation or a fetus pronounced dead at time of birth. For workers in the Photo and Diffusion groups, only pregnancies

occurring after date of first employment at Hudson were considered in the following presentation of results since prior pregnancy outcomes would not be attributable to Hudson occupational exposures. For the Non-exposed group, however, all pregnancies were considered. This was done to enhance the precision with which quantitative comparisons could be made and to make the age distribution more comparable between the groups. Prior work histories were reviewed to ensure that these non-exposed employees did not have former occupations which involved substantial chemical exposures.

Miscarriage ratios were calculated as the number of fetal losses prior to 28 weeks gestation divided by the number of total pregnancies. The miscarriage ratios identified for females in the Photolithographic, Diffusion, and Non-exposed group are given in Table 2 and are 31.3%, 38.9%, and 17.8%, respectively. While neither comparison involving the Photo group was statistically significant, the relative risks indicated that the occurrence of miscarriage in the Photolithographic group was elevated relative to the Non-exposed pregnancies but lower than that in the Diffusion pregnancies. Since a hypothesized true risk of miscarriage among women exposed to chemicals in the diffusion areas could not be discarded, and DEC management was also interested in Diffusion group potential risks, the miscarriage ratio in the Diffusion group was compared to that in the Non-exposed group with the result being a significant increase in risk (RR = 2.18; 95% confidence interval 1.18, 4.04).

The mean lengths of gestation for the miscarriages by group are presented in Table 3. The Diffusion group miscarriages occurred earlier than those in the other two groups. The differences between the groups were found to be of borderline statistical significance ( $F = 2.630$ ;  $p = 0.079$ ).

Because of the importance of age at time of pregnancy and gravidity to the potential of adverse pregnancy outcomes, these variables were next investigated. Mother's age at time of pregnancy was quite similar between the exposure groups. Nevertheless, due to its importance as a potential confounding variable it was included as a control variable in multivariate procedures which followed. The specific nature of the distribution of mother's age at time of pregnancy by group is shown in Table 4.

When the distribution of miscarriages was examined by exposure grouping across levels of gravidity the numbers arising in the different strata were too small to be conclusive. Nevertheless, the Non-exposed group was observed to have the lowest miscarriage ratio in each strata. Also, a general trend of increasing risk with increased gravidity, uncontrolled for age, was noted for each group (Table 5). For this reason gravidity was also included in subsequent multivariate analyses.

TABLE 2

## PREGNANCY OUTCOME AMONG FEMALE EMPLOYEES BY EXPOSURE GROUP

EXPOSURE GROUP	ABORTIONS		STILLBIRTHS		MISCARRIAGES		LIVEBIRTHS	
	N	RATIO	N	RATIO	N	RATIO	N	RATIO
PHOTO	2	(12.5)	0	(0.0)	5	(31.3)	9	(56.3)
DIFFUSION	1	(5.6)	0	(0.0)	7	(38.9)	10	(55.6)
NONEXPOSED	35	(8.8)	2	(0.5)	71	(17.8)	290	(72.9)

Ratio expressed as a number of events per 100 pregnancies.

Relative risk of miscarriage comparing Photo to Nonexposed women = 1.75; 95% CIE = (0.82, 3.73).

Relative risk of miscarriage comparing Diffusion to Nonexposed women = 2.18; 95% CIE = (1.18, 4.04).

Relative risk of miscarriage comparing combined exposure groups (Photo + Diffusion) to Nonexposed women = 1.98; 95% CIE = (1.20, 3.27).

TABLE 3

## DISTRIBUTION OF GESTATIONAL AGE (WEEKS) FOR MISCARRIAGES OCCURRING AMONG FEMALE DEC EMPLOYEES

PARAMETER	PHOTO	DIFFUSION	NONEXPOSED	ANOVA
MEAN	10.2	6.3	11.6	F = 2.630
STD. DEV.	2.49	1.38	6.31	p = 0.079
95% CIE	(7.1, 13.3)	(5.0, 7.6)	(10.1, 13.1)	
RANGE	6.0, 12.0	4.0, 18.0	1.0, 28.0	
MEDIAN	11.0	6.3	11.5	
NUMBER	5	7	71	

To determine whether the observed relative risks could have been due to a pre-existing difference in miscarriage risk between groups, pregnancies occurring prior to occupational exposure at the DEC facility were examined. In Table 6 the miscarriage ratio for each of the exposure groups is presented. In general, the miscarriage ratio was quite similar between the groups, with the highest rate found in Non-exposed women (16.8 per 100 pregnancies). However, as demonstrated in Table 7, these women were older, on average, at time of pregnancy.

TABLE 4

DISTRIBUTION OF AGE AT TIME OF PREGNANCY  
FOR FEMALE EMPLOYEES

PARAMETER	PHOTO	DIFFUSION	NONEXPOSED	ANOVA
MEAN	25.5	26.0	25.5	F = 0.112
STD. DEV.	3.28	4.10	4.50	p = 0.895
95% CIE	(23.8, 27.3)	(23.9, 28.1)	(25.1, 25.9)	
RANGE	19.8, 30.1	18.4, 33.3	16.1, 39.9	
MEDIAN	25.7	25.7	25.1	
NUMBER	16	18	398	

TABLE 5

MISCARRIAGES EXAMINED BY GRAVIDITY AND EXPOSURE GROUP

EXPOSURE GROUP	GRAVIDITY = 1		GRAVIDITY=2 OR 3		GRAVIDITY > 3	
	MIS.* N	TOTAL PREGS	MIS. N	TOTAL PREGS	MIS. N	TOTAL PREGS
PHOTO	2 (33.3)	6	3 (30.0)	10	-	-
DIFFUSION	1 (16.7)	6	3 (33.3)	9	3 (100.0)	3
NONEXPOSED	21 (14.0)	150	33 (19.1)	173	17 ( 22.7)	75

N represents the total number of miscarriages.

\* represents the number of miscarriages per 100 pregnancies.

While the observations are based on small numbers and may be unreliable, the relatively high reported frequency of induced abortion among the Photo and Diffusion females deserves mention, especially in light of its potential as a risk factor for subsequent miscarriage. Analyses specific to the women reporting miscarriages, however, found no indication for this as a substantial confounder (1 prior induced abortion among the Photo women who reported five miscarriages and 2 prior induced abortions among the Diffusion women who reported 7 miscarriages).

The use of prenatal care by the women reporting miscarriages was not found to differ meaningfully from women not reporting them.

TABLE 6

PREGNANCIES OCCURRING PRIOR TO DEC EMPLOYMENT AMONG  
FEMALE EMPLOYEES

EXPOSURE GROUP	ABORTIONS		STILLBIRTHS		MISCARRIAGES		LIVEBIRTHS	
	N	RATIO	N	RATIO	N	RATIO	N	RATIO
PHOTO	4	(50.0)	0	(0.0)	1	(12.5)	3	(37.5)
DIFFUSION	3	(50.0)	0	(0.0)	1	(16.7)	2	(33.3)
NONEXPOSED	30	(8.5)	2	(0.6)	59	(16.8)	261	(74.1)

Ratio expressed as a number of events per 100 pregnancies.

Relative risk of miscarriage comparing Photo to Nonexposed women = 0.75; 95% CIE = (0.12, 4.73).

Relative risk of miscarriage comparing Diffusion to Nonexposed women = 0.99; 95% CIE = (0.16, 6.04).

Relative risk of miscarriage comparing combined exposure groups (Photo + Diffusion) to Nonexposed women = 0.85; 95% CIE = (0.23, 3.14).

TABLE 7

DISTRIBUTION OF AGE AT TIME OF PREGNANCY FOR PREGNANCIES  
OCCURRING PRIOR TO DEC EMPLOYMENT

PARAMETER	PHOTO	DIFFUSION	NONEXPOSED	ANOVA
MEAN	20.9	20.7	25.0	F = 6.330
STD. DEV.	2.79	4.08	4.38	p = 0.002
95% CIE	(18.5, 23.2)	(16.5, 25.0)	(24.6, 25.5)	
RANGE	18.3, 26.7	16.1, 25.4	16.1, 39.9	
MEDIAN	19.3	18.3	24.4	
NUMBER	8	6	352	

A three stage approach was used to examine the potential effect of other risk factors. In the first stage a model was used which estimated the odds ratio for the other potential risk factors. The risk factors examined were: (1) mother's age at pregnancy, (2) gravidity, (3) consumption of caffeine containing beverages (coffee, hot or cold tea, colas), (4) amount of caffeine containing beverages consumed, (5) smoking during pregnancy and (6) consumption of alcoholic beverages during pregnancy. The results of this stage of the analysis are presented in Table 8.

In the second stage of this analysis, logistic regression models were fit which yielded estimates of the odds ratio for occupational exposure controlling for various combinations of the six potential risk factors examined in the first stage. The results of the second stage are presented in Table 9. In the third stage, the two exposed groups were combined and the same analyses repeated. These results are in Table 10.

The estimated odds ratios for the six models in Table 8 show that none is significantly associated with the outcome, miscarriage. In this table two odds ratios have been provided for mother's age, one for a one year increase and a second for a five year increase in age. The variable gravidity was categorized into three groups and analyzed via two design variables which were set up to yield the comparisons stated in Table 8. Based on these estimated odds ratios, there is no strong evidence for potential confounding, except for mother's age. However, to be certain, models addressing this issue were fit.

TABLE 8  
ESTIMATED ODDS RATIOS AND CONFIDENCE INTERVAL ESTIMATES  
FOR CONTROL VARIABLES

MODEL	CONTROL VARIABLE	OR	95% CIE FOR OR
1	AGE AT PREGNANCY: 1 YEAR	1.03	(0.98, 1.09)
	5 YEARS	1.17	(0.89, 1.55)
2	GRAVIDITY:		
	2nd or 3rd vs 1st	1.29	(0.73, 2.28)
	4th or more vs 1st	1.74	(0.89, 3.43)
3	CAFFEINE USE DURING PREGNANCY (yes, no)	0.80	(0.42, 1.55)
4	AMOUNT OF CAFFEINE USE DURING PREGNANCY (2 cup increase)	1.03	(0.79, 1.34)
5	SMOKING DURING PREGNANCY (yes, no)	1.02	(0.61, 1.72)
6	ALCOHOL CONSUMPTION DURING PREGNANCY (yes, no)	0.74	(0.42, 1.31)

The results of fitting seven different logistic regression models are presented in Table 9. The odds ratios presented are based on the estimated coefficients for two design variables used to represent the three categories of occupational exposure. The design variables were formed to yield the stated comparisons of Photo vs Nonexposed and Diffusion vs Nonexposed.

Thus, the estimated logistic regression coefficients when exponentiated, provide an estimate of the odds ratios of Photo vs Nonexposed and Diffusion vs Nonexposed controlling for any other variables in the model. The information in Table 9 is presented in 7 rows and 8 columns. Each row denotes a particular model whose number is given in column 1. Column 2 contains the control variables being examined. The estimated odds ratio for Photo vs Nonexposed is in column 3 and the endpoints of the 95% confidence interval are given in columns 4 and 5. Column 6 contains the estimated odds ratio for the Diffusion vs Nonexposed comparison while columns 7 and 8 contain the endpoints of the 95% confidence interval estimate.

The results presented in Table 9 show that for the comparison between Photo and Nonexposed the estimated odds ratios (column 3) range from 2.27 to (model 1) to 2.89 (model 5). Although each of these is elevated above 2.0, the lower limit of the confidence interval (column 4) is less than 1.0 indicating that each is not statistically significantly different from 1.0. The consistency of these estimates is noteworthy and supports the previous observation that none of these control variables is a strong confounder of the occupational exposure.

The odds ratios for the Diffusion vs Nonexposed (column 6) range from 2.80 to 3.42. Each is not only greater than 2.0 but each is statistically significantly different from 1.0. Thus, the previously noted significant association between miscarriage and Diffusion exposure remains in the presence of controlling variables. The consistency of both the individual estimates and the confidence intervals shows that the control variables are not confounding the association.

Table 10 presents the results of the third stage of the multivariate analysis. The estimated odds ratios in Table 10 were obtained by exponentiating the coefficient for the design variable for exposure when Photo and Diffusion were combined. The same control variables (models) used in Table 9 are represented. The estimated odds ratios range from 2.58 (model 1) to 3.17 (model 5) and lie, as one would expect, between the values in columns 3 and 6 of Table 9. In each case, they are statistically significantly different from 1.0. This analysis was not done to achieve an increase in analytic power but rather to gain an estimate of the overall risk among the fab employees studied. Since there is scant laboratory and animal evidence regarding exposure to specific chemicals and risk of human reproductive failure and since the direction of the risk estimates for the two exposed groups was the same, it was felt that an overall risk measure could be useful.

TABLE 9

CRUDE AND ADJUSTED ODDS RATIOS FOR THE RISK OF MISCARRIAGE COMPARING PHOTO OR DIFFUSION  
TO NONEXPOSED WOMEN

MODEL (1)	CONTROL VARIABLE (2)	PHOTO VS NONEXPOSED			DIFFUSION VS NONEXPOSED		
		OR (3)	95% CIE FOR OR (4)	OR (5)	OR (6)	95% CIE FOR OR (7)	OR (8)
1	CRUDE UNADJUSTED ANALYSIS	2.27	(0.74, 6.98)		2.86	(1.05, 7.78)	
2	EXPOSURE, CONTROLLING FOR AGE AT PREGNANCY	2.32	(0.75, 7.16)		2.80	(1.03, 7.62)	
3	EXPOSURE, CONTROLLING FOR AGE AT PREGNANCY AND GRAVIDITY (1, 2 OR 3, 4+)	2.51	(0.81, 7.82)		2.89	(1.06, 7.92)	
4	EXPOSURE, CONTROLLING FOR AGE AT PREG., GRAVIDITY AND CAFFEINE USE DURING PREGNANCY (yes, no)	2.81	(0.90, 8.79)		3.25	(1.18, 8.95)	
5	EXPOSURE, CONTROLLING FOR AGE AT PREG., GRAVIDITY AND AMOUNT OF CAFFEINE USE DURING PREGNANCY (cups of beverage)	2.89	(0.92, 9.03)		3.42	(1.23, 9.53)	
6	EXPOSURE, CONTROLLING FOR AGE AT PREG., GRAVIDITY AND SMOKING DURING PREGNANCY (yes, no)	2.81	(0.90, 8.79)		3.30	(1.20, 9.10)	
7	EXPOSURE, CONTROLLING FOR AGE AT PREG., GRAVIDITY AND ALCOHOL CONSUMPTION DURING PREGNANCY (yes, no)	2.76	(0.88, 8.61)		3.19	(1.16, 8.83)	

TABLE 10

CRUDE AND ADJUSTED ODDS RATIOS FOR THE RISK OF MISCARRIAGE  
COMPARING EXPOSED (PHOTO + DIFFUSION) TO NONEXPOSED WOMEN

MODEL (1)	CONTROL VARIABLE (2)	OR (3)	95% C I E FOR OR (4) (5)
1	CRUDE UNADJUSTED ANALYSIS	2.58	(1.20, 5.56)
2	EXPOSURE, CONTROLLING FOR AGE AT PREGNANCY	2.58	(1.19, 5.56)
3	EXPOSURE, CONTROLLING FOR AGE AT PREGNANCY AND GRAVIDITY (1, 2 OR 3, 4+)	2.72	(1.25, 5.91)
4	EXPOSURE, CONTROLLING FOR AGE AT PREG., GRAVIDITY AND CAFFEINE USE DURING PREGNANCY (yes, no)	3.05	(1.39, 6.67)
5	EXPOSURE, CONTROLLING FOR AGE AT PREG., GRAVIDITY AND AMOUNT OF CAFFEINE USE DURING PREGNANCY (cups of beverage)	3.17	(1.44, 6.96)
6	EXPOSURE, CONTROLLING FOR AGE AT PREG., GRAVIDITY AND SMOKING DURING PREGNANCY (yes, no)	3.07	(1.41, 6.72)
7	EXPOSURE, CONTROLLING FOR AGE AT PREG., GRAVIDITY AND ALCOHOL CONSUMPTION DURING PREGNANCY (yes, no)	2.99	(1.37, 6.56)

Other Control Variables

In order to determine the need for further multivariate analysis, a variety of other potential control variables were analyzed with respect to their relationship with exposure status and pregnancy outcome. Demographic variables for which no differences warranting further analysis were observed included marital status, ethnicity, education, and religious preference. Answers to questions concerning chemical exposures at home,

though not restricted to time of pregnancy, were examined but none were evidenced to vary significantly between the groups. These included exposure to chemical lawn treatments; use of pesticides or herbicides; use of home cleaning fluids such as floor cleaners, wax strippers, and furniture refinishers; regular hobby use of paint, varnish, solvents, paint strippers, degreasers, lead, adhesives and glues; use of artificial sweeteners such as saccharin; and reporting of husband's exposure to Agent Orange while serving in the armed forces.

Similarly, the use of contraceptive creams, foams or jelly around the time of conception was examined by exposure group but not found to differ meaningfully. Complications during pregnancy, including high blood pressure, hematuria, nausea and vomiting, toxemia, placental problems, exposure to rubella, Rh incompatibility, urinary tract infections, incompetent cervix, vaginal bleeding or spotting, premature rupture of the membranes, premature labor, and exposure to influenza in the first trimester were also investigated but not found to differ between groups.

Other reproductive outcomes studied included reported infertility, birth weight and pre-term delivery. None of these outcomes was found to differ significantly between the groups. The number of female employees reporting difficulty becoming pregnant was two (3.0%) in the Photo exposure group, one (1.5%) in the Diffusion group, and three (0.9%) among Non-exposed women. For spouses of male employees, two individuals in each occupational group reported having such difficulties (2.9% Photo, 2.2% Diffusion and 1.8% Non-exposed. These differences were not found to be statistically significant but are, of course, too small to be considered as truly reliable estimates of infertility risk. There was a striking degree of similarity in birth weights for pregnancies occurring in the different exposure groups. The mean and median birth weight and standard deviations are displayed in Table 11 in pounds and grams. The occurrence of

TABLE 11

DISTRIBUTION OF INFANT'S BIRTH WEIGHT BY EXPOSURE GROUP FOR FEMALE EMPLOYEES

PARAMETER	PHOTO	DIFFUSION	NONEXPOSED	ANOVA
MEAN (pounds)	7.56	7.38	7.24	F = 0.279
STD. DEV.	1.04	1.09	1.36	p = 0.756
MEDIAN	7.44	7.22	7.37	
MEAN (GRAMS)	3427.1	3348.1	3285.7	
STD. DEV.	472.14	495.99	615.59	
MEDIAN	3373.6	3274.4	3340.5	
NUMBER	10	10	286	

pre-term deliveries was reported in only a small proportion of pregnancies. No pre-term deliveries occurred among Photo pregnancies and only one was indicated in the Diffusion group. For Non-exposed women, a total of 21 or 7.6% of their livebirths were considered by themselves to be pre-term. These differences were not statistically significant.

The reported prevalence of congenital anomalies did not indicate any quantitative relationship with exposure group, but the number of such reports was small. A list of the anomalies reported is found in Appendix I.

The examination of specific exposure histories of the women reporting miscarriages in the manufacturing groups is a useful adjunct to the population based analysis of this study. This is especially true in light of the small number of miscarriages observed. Several considerations are important in reviewing the information presented in Table 12. First, recall of specific work stations was described to the best of the respondents ability. Second, workers usually had responsibilities which brought them to a large number of stations during a typical work day and the quantification of their work station exposures as a function of the proportion of a day spent there was usually imprecise. Third, information collected about chemical handling and mixing, repairing or cleaning machines, involvement in cleaning-up chemical spills, use of protective devices, and other practices in the fab area were collected in reference to each of their jobs but cannot be precisely linked to dates of reproductive or other health events. For each of these activities, however, the proportion of time spent on each was recorded.

Of the four Photo women experiencing five miscarriages while at Hudson, two were technicians, one was a process engineer and one was a work coordinator. The median duration of employment prior to miscarriage was 12 months. Of the five Diffusion women experiencing seven miscarriages, four were operators and one was an engineering assistant. In this group the median duration of employment prior to miscarriage was 15 months.

TABLE 12

## CASE REPORTS OF WORK HISTORY AND PREGNANCY INFORMATION FOR EXPOSED WOMEN WHO REPORTED HAVING A MISCARRIAGE

SUBJECT	EXPOSURE GROUP* CLASSIFICATION	TOTAL NO. PREGS.	DATE MISC.	GESTATIONAL AGE (weeks)	UNDER PHYSICIAN'S CARE AT TIME OF MISCARRIAGE	JOB CATEGORY AT TIME OF MISCARRIAGE	LENGTH EMP PRIOR TO PREGNANCY	PRIOR FACILITY EMP
1	PHOTO	2 (1 pre- facility 1 post)	7/79 +	6	No	Work Coordinator 2/79-1/81	5 months	None
Involved in handling and mixing chemicals and cleaning of equipment - wore protective gear, but no respirator; spent 8 hours/day in fab area.								
2	PHOTO	3 (1 pre- facility 2 post)	8/84	12	Yes	Technician 6/83-12/84	14 months	Operator 2/80-6/83 28 months 1 year spent outside fab
Involved in chemical mixing and handling - wore protective gear but not respirator; 6 hours/day spent in fab area.								
3	PHOTO	1 (1 post- facility)	7/81	11	Yes	Technician 7/80-11/84	12 months	None
Involved in mixing and handling chemicals, and cleaning equipment, spill cleanup, and equipment repair - wore protective gear (no respirator); on average 8 hours/day spent in fab area.								
4	PHOTO	2 (2 post- facility)	3/83	12	Yes	Process Engineer 6/82-7/84	9 months	None
Works with chemicals in fab area and also was involved in cleaning equipment and machines - wore protective gear; sometimes involved in spill cleanup; on average 5 hours/day spent in fab area.								
4	PHOTO	2 (2 post- facility)	8/83	10	Yes	Process Engineer 6/82-7/84	14 months	None
Same as above.								

\* Job title and work station information, collected during the interview, was used to classify exposure group. All workers reporting involvement in equipment cleaning, chemical mixing, and chemical spill clean-up, reported doing this for less than 20% of their work time.

+ Miscarriage occurred while working for the company in leased space prior to opening of the main facility. The manufacturing process and materials used during this period were identical to those at permanent location.

TABLE 12 - continued

SUBJECT	EXPOSURE GROUP* CLASSIFICATION	TOTAL NO. PREGS.	DATE MISC.	GESTATIONAL AGE (weeks)	UNDER PHYSICIAN'S CARE AT TIME OF MISCARRIAGE	JOB CATEGORY AT TIME OF MISCARRIAGE	LENGTH EMP PRIOR TO PREGNANCY	PRIOR FACILITY EMP
5	DIFFUSION	3 (3 post facility)	5/82	8	Yes	Diffusion Operator 2/80-5/82	27 months	None
Involved in mixing and handling chemicals, and cleaning sinks - wore protective gear but not respirator.								
6	DIFFUSION	4 (1 pre- facility 3 post)	5/84	4	No	Custom Fab Operator 3/81-12/84	38 months	MOS Fab Operator 1979-3/81 18 months
Except for respirator, wore protective gear; spends 7 hours/day in fab area.								
6	DIFFUSION	4 (1 pre- facility 3 post)	8/84	6	Yes	Custom Fab Operator 3/81-12/84	41 months	MOS Fab Operator 1979-3/81 18 months
Same as above.								
7	DIFFUSION	3 (1 pre- facility 2 post)	4/79 +	8	No	Operator 3/79-12/84	1 month	None
Involved mixing and handling chemicals and cleaning of equipment - wore protective gear while working with chemicals, including respirator; 8 hours/day spent in fab area.								
8	DIFFUSION	5 (3 pre- facility 2 post)	7/84	6	Yes	Operator 7/83-12/84	12 months	None
Involved in mixing chemicals and cleaning equipment - wears protective gear but not respirator; 8 hours/day spent in fab; up to 2 hours over-time per week spent in fab area.								
8	DIFFUSION	5 (3 pre- facility 2 post)	10/84	6	Yes	Operator 7/83-12/84	15 months	None
Same as above.								
9	DIFFUSION	2 (2 post facility)	6/83	6	Yes	Engineer Assistant 1/83-6/83	6 months	None
Involved in mixing and handling chemicals and cleaning equipment - wore protective gear but not respirator; spent an average of 4 hours/day in fab area.								

\* Job title and work station information, collected during the interview, was used to classify exposure group. All workers reporting involvement in equipment cleaning, chemical mixing, and chemical spill clean-up, reported doing this for less than 20% of their work time.

+ Miscarriage occurred while working for the company in leased space prior to opening of the main facility. The manufacturing process and materials used during this period were identical to those at permanent location.

Reproductive Outcomes: Males

Among spouses of male employees, the miscarriage ratios were based on relatively small numbers of events and were generally low in all three groups (Table 13). They ranged from 5.3 per 100 pregnancies in the Non-exposed group to 12.5 per 100 pregnancies in the Photo exposure group; these differences were not statistically significant. When age at time of pregnancy was examined it was found to be similar for the groups (Table 14). Numbers being small, the miscarriage ratios by gravidity are not stable but, are presented in Table 15.

TABLE 13  
PREGNANCY OUTCOME AMONG SPOUSES OF MALE EMPLOYEES,  
BY EXPOSURE GROUP

EXPOSURE GROUP	ABORTIONS		STILLBIRTHS		MISCARRIAGES		LIVEBIRTHS	
	N	RATIO	N	RATIO	N	RATIO	N	RATIO
PHOTO	0	( 0.0)	0	( 0.0)	2	(12.5)	14	(87.5)
DIFFUSION	0	( 0.0)	0	( 0.0)	1	( 7.7)	12	(92.3)
NONEXPOSED	1	( 5.3)	0	( 0.0)	1	( 5.3)	17	(89.5)

Ratio expressed as a number of events per 100 pregnancies.

Relative risk of miscarriage comparing Photo to Nonexposed women = 2.38; 95% CIE = (0.24, 23.84).

Relative risk of miscarriage comparing Diffusion to Nonexposed women = 1.46; 95% CIE = (0.10, 21.33).

Relative risk of miscarriage comparing combined exposure groups (Photo + Diffusion) to Nonexposed women = 1.97; 95% CIE = (0.22, 17.53).

TABLE 14  
DISTRIBUTION OF AGE AT TIME OF PREGNANCY FOR SPOUSES OF  
MALE EMPLOYEES

PARAMETER	PHOTO	DIFFUSION	NONEXPOSED	ANOVA
MEAN	26.1	29.2	28.5	F = 1.676
STD. DEV.	4.92	5.28	4.62	p = 0.199
95% CIE	(23.5, 28.8)	(25.0, 32.4)	(26.3, 30.7)	
RANGE	19.5, 35.0	22.5, 41.6	21.6, 35.2	
MEDIAN	24.1	29.0	28.9	
NUMBER	16	13	19	

TABLE 15

MISCARRIAGES EXAMINED BY GRAVIDITY FOR PREGNANCIES WHICH  
OCCURRED AMONG SPOUSES OF MALE EMPLOYEES

EXPOSURE GROUP	GRAVIDITY = 1		GRAVIDITY=2 OR 3		GRAVIDITY > 3	
	MIS.* N	TOTAL PREGS	MIS. N	TOTAL PREGS	MIS. N	TOTAL PREGS
PHOTO	0 ( 0.0)	6	1 (14.3)	7	1 ( 33.3)	3
DIFFUSION	0 ( 0.0)	7	0 ( 0.0)	5	1 (100.0)	1
NONEXPOSED	0 ( 0.0)	10	1 (11.1)	9	-	-

N represents the total number of miscarriages.

\* represents the number of miscarriages per 100 pregnancies.

Miscarriage ratios prior to husband's employment at DEC Hudson, were examined. Again, numbers are small, however, no meaningful differences were observed.

#### General Health Outcomes

The objective of calculating the prevalence of various self-reported illness symptoms was to identify any potential work-related problems for future follow-up rather than to attempt analytic assessment of potential causal relationships. Respondents were asked about a large number of illness symptoms which might have been experienced during the last five years, the period roughly corresponding to the existence of the Hudson facility. The first analysis examined, in a cross-sectional fashion, the reported prevalence as it related to occupational group. A subsequent analysis examined prevalence in light of symptoms' temporal relationships to employment. It should be noted, however, that this type of coupling of work history to retrospectively reported symptoms, most of which are episodic in nature, is not able to provide the type of information required to distinguish a cause from a correlation. Prevalence is rarely the measure of choice when etiologic research about chronic disease is the objective. It is a function of survivorship as well as disease incidence. For non-lethal symptoms with no clear moment of onset, prevalence is a convenient measure with which to describe an exposure/symptom relationship.

Before calculating prevalence ratios by exposure, the occupational groups (Photo, Diffusion, and Non-exposed) were examined for differences in a variety of variables in order to determine whether any differences would need to be controlled for in subsequent analyses. There were few meaningful differences between the groups, although a significant difference was found

In level of education for both men and women, with the levels being highest in the Non-exposed group. Education was, therefore, further considered as a potential confounding variable. Among females, weight in pounds, and weight divided by height in inches (as a simple measure of obesity) was also found to differ modestly. Specifically, Diffusion group females had a higher mean value for both variables than did the Non-exposed subjects; this was also further considered in subsequent analyses.

The results of the first data analysis, presented in the form of prevalence ratios are given in Appendix II. The individual tables for each symptom report the prevalence ratios by exposure (Photo vs Non-exposed, Diffusion vs Non-exposed, and Photo + Diffusion vs Non-exposed). They are presented for both sexes combined and stratified by sex.

There were no significant associations found between exposure and reported symptom prevalence overall or for either sex, for slipped disk, high blood pressure, cancer, thyroid problems, gall bladder problems, respiratory problems, kidney problems, seizure disorders, anemia, dizziness or eyestrain. It should be acknowledged that the likelihood of identifying one or more elevated risks is increased when searching among a large number of outcomes, as this study did. Furthermore, the numbers of individuals who reported symptoms is sometimes too small to be followed by detailed analysis, or to lead to scientific inference. A simple statistical approach to reporting this prevalence belies this fact.

A summary of the significant associations is presented in Table 19. Symptoms which were reported more frequently among an exposure group than among the Non-exposed included: frequent or severe headache (Diffusion females), frequent or severe sore throat (Photo and Diffusion females), frequent or severe nausea (Photo females and Diffusion males), frequent or severe rash (Photo females), and arthritis (Photo females). Additionally, Diffusion females reported back problems (other than slipped disc) less frequently than Non-exposed females but numbers were rather small in this analysis. The reports of diabetes are far too few to be evaluated more formally or to infer any association with occupational exposure. Also, as seen below, diabetes was not temporally related with employment at Hudson.

The relationship between each of these reported symptoms and other variables that could have potentially confounded the results was examined. Associations of potential confounders with symptoms or exposure group were further controlled for using multiple logistic regression. These variables included age, education, weight, and a variety of other variables including current use of caffeine, alcohol, cigarettes, and sugar substitutes; number of pregnancies and history of oral contraceptive use (females only); chemical lawn treatment; use of floor cleaners and pesticides; home termite treatment; and hobby

exposure to paint, varnish, solvent, paint stripper, degreasers, and lead.

The results of these multivariate analyses are presented in Table 20 and variables used in the adjustment are identified in the table footnotes. Multivariate results are not presented for diabetes since the numbers were considered too small to yield reliable estimates. Potential confounding variables were identified by examining their relationship with reported symptom and exposure group. Variables found to require further analysis were included in multiple logistic regression models. It is apparent that after adjusting for potentially confounding variables, there continued to exist statistically significant associations between occupational exposure groups and the reporting of certain general health symptoms.

Since respondents were asked about the duration of most reported symptoms, an analysis examining the temporal relationship between symptoms and occupation at Hudson was also performed. The analysis including illness symptoms only if they did not report having them prior to first Hudson employment is presented in Table 21. This summary table reports the symptoms, reported by exposure group and sex, whose onset was after first Hudson employment.

While some modest changes were observed, the same caution about relatively small numbers of events and an arguable lack of biological plausibility for an association (e.g. arthritis) must be raised. The possibility that one or more of the associations is artifactual should also be further considered.

TABLE 16

DISTRIBUTION OF SELECTED DEMOGRAPHIC VARIABLES BY EXPOSURE GROUP

VARIABLE	PHOTO	DIFFUSION	NONEXPOSED
<b>SEX</b>			
% male	50.7	57.6	25.1
% female	49.3	42.4	74.9
<b>RELIGION</b>			
% Catholic	56.7	58.9	54.6
% Protestant	27.6	30.5	27.9
% other	15.7	10.7	17.5
Chi square=4.04, d.f.=4, p=.3947			
<b>ETHNIC GROUP</b>			
% white	94.0	94.8	92.1
% other	6.0	5.2	7.9
Chi square=1.59, d.f.=2, p=.4529			
<b>MARITAL STATUS</b>			
% never married	30.1	34.4	29.6
% currently married	57.4	56.7	54.0
% formerly married	12.5	8.8	16.5
Chi square=6.18, d.f.=4, p=.1862			

TABLE 17

DESCRIPTIVE STATISTICS FOR SELECTED DEMOGRAPHIC VARIABLES  
BY EXPOSURE GROUP FOR MALE SUBJECTS ONLY

VARIABLE	PHOTO	DIFFUSION	NONEXPOSED	F RATIO	P-VALUE
<b>AGE</b>					
mean	29.3	30.0	31.2	1.67	0.1909
SD	6.3	7.5	7.3		
<b>EDUCATION</b>					
mean	14.1*	13.8*	15.2	13.08	0.0000
SD	2.0	2.0	2.4		
median	13.9	13.6	15.6		
<b>SPOUSE'S TOTAL PREGNANCIES (1)</b>					
mean	2.3	1.6	1.7	2.23	0.1119
SD	1.9	1.5	1.4		
median	2.4	1.5	1.7		
<b>WEIGHT (LBS)</b>					
mean	181.0	178.0	176.0	0.55	0.5772
SD	31.9	24.2	29.6		
<b>WEIGHT/HEIGHT</b>					
mean	2.5	2.5	2.5	0.53	0.5893
SD	0.40	0.31	0.38		

\* Significant difference (0.05 level) in means between exposed and nonexposed groups.

(1) Only for those men who were married at some time.

TABLE 18

DESCRIPTIVE STATISTICS FOR SELECTED DEMOGRAPHIC VARIABLES  
BY EXPOSURE GROUP FOR FEMALE SUBJECTS ONLY

VARIABLE	PHOTO	DIFFUSION	NONEXPOSED	F RATIO	P-VALUE
<b>AGE</b>					
mean	33.9	33.2	34.2	0.29	0.7510
SD	11.1	11.4	9.0		
<b>EDUCATION</b>					
mean	12.8*	12.5*	14.4	27.46	0.0000
SD	1.8	1.9	2.4		
median	12.2	12.1	14.1		
<b>TOTAL PREGNANCIES (1)</b>					
mean	2.2	2.6	2.0	2.32	0.1000
SD	1.9	1.9	1.9		
median	1.9	2.3	1.7		
<b>WEIGHT (LBS)</b>					
mean	135.0	146.0*	137.0	3.74	0.0245
SD	25.0	30.9	24.4		
<b>WEIGHT/HEIGHT</b>					
mean	2.1	2.3*	2.1	3.82	0.0225
SD	0.38	0.44	0.36		

\* Significant difference (0.05 level) in means between exposed and nonexposed groups.

(1) Only for those women who were married at some time.

TABLE 19

SUMMARY TABLE FOR SYMPTOMS SIGNIFICANTLY ASSOCIATED \*  
WITH EXPOSURE, BY SEX GROUP

EXPOSURE GROUP	REPORTED SYMPTOM	REPORTING SYMPTOMS				PREVALENCE RATIO	95% CIE (LL, UL)
		EXPOSED N	%	NONEXPOSED N	%		
<b>FEMALES</b>							
DIFFUSION	HEADACHE	31	47.0	73	21.7	2.16	1.56, 3.00
DIFFUSION	OTHER BACK PROBLEMS	6	9.1	72	21.4	0.42	0.19, 0.94
DIFFUSION	SORE THROAT	8	11.9	13	3.9	3.07	1.32, 7.11
PHOTO	ARTHRITIS	10	15.9	23	6.8	2.32	1.16, 4.63
PHOTO	DIABETES**	3	4.5	2	0.6	7.55	1.29, 44.29
PHOTO	NAUSEA	7	10.6	12	3.6	2.94	1.20, 7.20
PHOTO	RASH	9	13.4	19	5.7	2.38	1.12, 5.02
PHOTO	SORE THROAT	7	10.6	13	3.9	2.73	1.13, 6.57
<b>MALES</b>							
DIFFUSION	NAUSEA	7	7.9	1	0.9	8.73	1.09, 69.65

\* A symptom with a prevalence ratio whose confidence interval estimate does not include 1.0.

\*\* Numbers too small to be reliable.

TABLE 20

ESTIMATED ODDS RATIOS ADJUSTED FOR POTENTIAL CONFOUNDING  
VARIABLES \*

EXPOSURE GROUP	REPORTED SYMPTOM	SEX GROUP	ODDS RATIO	95% CIE (LL, UL)	METHOD
PHOTO	ARTHRITIS	FEMALES	2.57 2.64	(1.16, 5.70) (1.10, 6.31)	CRUDE ADJUSTED+ (1)
PHOTO	DIABETES	FEMALES	7.85 5.48	(1.29, 49.93) (2.06, 14.59)	CRUDE ADJUSTED (2)
PHOTO	RASH	FEMALES	2.59 2.80	(1.12, 6.00) (1.19, 6.60)	CRUDE ADJUSTED (3)
DIFFUSION	OTHER BACK PROBLEMS	FEMALES	0.37 0.43	(0.15, 0.88) (0.18, 1.05)	CRUDE ADJUSTED (4)
DIFFUSION	HEADACHE	FEMALES	3.19 3.27	(1.84, 5.52) (1.86, 5.74)	CRUDE ADJUSTED (5)
DIFFUSION	NAUSEA	MALES	9.39 9.56	(1.13, 77.82) (1.13, 80.96)	CRUDE ADJUSTED (6)

\* Odds ratios adjusted for the distribution of other variables by the use of multiple logistic regression.

+ Potential confounding variables included in the model.

- (1) Adjusted for age, use of sugar substitutes, and number of pregnancies.
- (2) Adjusted for age and oral contraceptive use.
- (3) Adjusted for pesticide use and exposure to varnish and paint.
- (4) Adjusted for pesticide use and having home treated for termites.
- (5) Adjusted for use of oral contraceptives.
- (6) Adjusted for exposure to lead.

TABLE 21

SUMMARY TABLE FOR SYMPTOMS SIGNIFICANTLY ASSOCIATED TEMPORALLY  
WITH EXPOSURE, BY SEX GROUP\*

EXPOSURE GROUP	REPORTED SYMPTOM	REPORTING SYMPTOMS				PREVALENCE RATIO	95% CIE (LL, UL)
		EXPOSED		NONEXPOSED			
		N	%	N	%		
<b>FEMALES</b>							
DIFFUSION	HEADACHE	31	47.0	73	21.7	2.16	1.56, 3.00
PHOTO	ARTHRITIS	5	7.9	7	2.1	3.81	1.25, 11.63
PHOTO	NAUSEA	7	10.6	12	3.6	2.94	1.20, 7.20
PHOTO	RASH	9	13.4	19	5.7	2.38	1.12, 5.02
PHOTO	SORE THROAT	6	9.1	11	3.3	2.76	1.06, 7.20
<b>MALES</b>							
DIFFUSION	NAUSEA	7	7.9	1	0.9	8.73	1.09, 69.65

\* A symptom with a prevalence ratio whose confidence interval estimate does not include 1.0.

## DISCUSSION

As with any study, the research findings of this investigation need to be interpreted in terms of the research objectives, methodologies employed, and the context in which it was conducted. Each of these considerations will be addressed.

### Research Objectives

Epidemiologic studies are conducted in order to increase knowledge about the risk factor/disease relationships they are intended to investigate. Studies which are subsequent to other carefully conducted works are generally more refined with respect to hypotheses and more specific with respect to data collection. This was not the case in the present study. Virtually no human data concerning exposures to chemicals of interest at the Hudson facility with respect to miscarriage are available. This effort was an important first step to actively research a health concern in a systematic way. In the absence of extensive qualitative or quantitative data on the potential mechanism or, indeed, the potential chemical or physical agent(s) involved, interpretation should be cautious.

The finding of the more elevated risk among the non-photolithographic group, was unexpected. However, given the lack of epidemiologic evidence for a relationship with miscarriage among either exposure group, and occupational histories for manufacturing workers which are self-reported and may be somewhat imprecise with respect to exposure, the findings can only lead to the conclusion that research follow-up is required.

### Methodologies Employed

As a first step, it was felt that what was needed was a careful observational study which would systematically count numerators and denominators, that is, the occurrence of health related events among the defined population at risk. In this light, response rates were reasonably high, and an attempt was made to identify and contact all former manufacturing workers. As expressed to the company this was important because workers who left employment might have had a higher adverse health experience (left because of illness or threatened illness) or a more favorable experience (left to care for young, healthy children), than those still in employment. Given the short history of the Hudson manufacturing facility, there were very few former workers to add to the current employees. Former production workers employed in other positions (non-exposed) at time of interview were, however, classified as to their exposure group at time of pregnancy outcome. Sampling was therefore, relatively complete, with the great majority of production workers and non-exposed females available at the facility,

Included in the study. The only fab workers not interviewed were those with less than one month work history before the initiation of interviews. With respect to collecting accurate information on reproductive histories, all methods available (interview, medical records, vital statistics, insurance records) may have some ascertainment bias, nevertheless, interview data has been cited as perhaps the single most useful source.(2)

Criteria for classification of exposure group were determined prior to data analysis from information supplied by DEC. Workers were allocated to Photo or Diffusion categories for analysis, based on objective criteria about predominant work stations and chemical exposures. Nevertheless, some workers reported work histories in a variety of production areas. If the harmful effect of some chemical agent could be realized at some time after first (or cumulative) exposure, then categorization of exposure group based on work history at time of pregnancy outcome may not be the most suitable criteria; future research should bear this in mind.

One of the most critical methodologic issues which bears on the interpretation of the results is the modest sample size. This was a function of the number of production workers employed and also of the relatively short history of the facility. Specifically, the miscarriage ratios were based on only 34 pregnancies in the manufacturing groups. Regardless of levels of statistical significance, ratios based on small numbers of events are more likely to change substantively when further observations are included. Two ways to increase the observations would be to 1) add workers who are now employed but were not at the time of data collection and/or 2) continue observing the reproductive experience of workers included in this study beyond the date of their interview.

A second issue influencing the interpretation of the results is the potential of recall bias. This issue was examined in two ways. The first was the potential for some over-reporting of adverse outcome by employees who felt threatened as a result of discussions concerning the potential for reproductive problems in an exposed group. If this were true, one might expect the over-reporting primarily in the photolithographic group where some concern had been expressed prior to the study and which was the focus of attention of management, not in the group with the highest proportion of reported miscarriages. In addition, there were no differences in the proportion of women in any group who reported spotting or bleeding during pregnancy (other than the miscarriage), or any other adverse reproductive event, indicating that any selective reporting would have to have been specific for this one single outcome. Finally, if the perceived risk had caused events such as spotting, bleeding, or other menstrual irregularities prior to a confirmed diagnosis of pregnancy to have been reported as miscarriages, the lower gestational age at pregnancy might have again been expected for the photolithographic rather than the diffusion group. In any event, the investigators, interviewers, and DEC management agreed

that there had been no widespread alarm about work related health effects prior to this study. Nevertheless, if some level of alarm was unrecognized, the potential for over-reporting of miscarriages and other health outcomes would remain a real concern. Similarly, if management/employee relations were deemed to be strained as a result of financial or other disputes the potential of such prevarication or exaggeration would have been of heightened concern; this was definitely not the case, however.

With respect to a potential bias due to including the Non-exposed reproductive experience prior to Hudson employment, studies in the published literature and our own quantitative analyses lead us to conclude against this as a factor which would alter the basic conclusions of this report.

In one study comparing questionnaire data to records of menstrual histories, Wilcox and Horney (3) found that 82% of documented miscarriages were recalled within 10 years, about 80% between 10-20 years, and about 73% prior to 20 years. The retrospective recall data were collected in a one page questionnaire with instructions to record pregnancies "as well as they could recall them", rather than by trained interviewers. Our interviewers, who were unaware of the central research question, were alerted to identify uncertainty in responses. Uncertain responses were then reported so that medical follow-up could be attempted. Furthermore, in the Wilcox study some miscarriages were recalled which had not been included in the recorded menstrual history. These authors acknowledge that a "false positive" report is a less plausible explanation than imperfection of the menstrual record. Such errors of omission in the recording system used by the authors suggest that other errors may have prevailed as well, and that recall might have been higher than estimated.

Another study examining recall of miscarriage, compared questionnaire reports with obstetrical records from the Mayo and Gunderson Clinics as well as from several physicians' practices in Boston, Houston, and Los Angeles.(4) As expected there were large amounts of missing data from medical records, therefore only pregnancies for which complete information was present were used in the comparison. Mail and telephone surveys were used to assess recall (again not as good as personal interview). Agreement was found to be "good to excellent" for reporting prior pregnancies, and "excellent" for reporting number of prior miscarriages as judged by the kappa statistic. Under-reporting was estimated as being at a maximum of ten percent. No differences were found in recall ability between a DES exposed group (presumably with heightened awareness) and all comparison groups.

One way to examine the potential that miscarriage recall was a function of the time since it occurred, in our data, was to analyze the miscarriage ratios occurring in the non-exposed group over time, while stratifying by age at conception. For reported pregnancy outcomes occurring within 20 years of the time of

interview, there is little evidence for a trend of miscarriage reporting with time period (Table 22). In fact, in cells where the ratios are more stable, the reporting of a miscarriage was slightly more frequent five to ten years ago (1975-79) than in the most recent five year period (women age 20 or older at time of conception). Additionally, in the largest group, ages 20 to 30 at conception, the ratio reported ten to twenty years ago (1963-74) was nearly identical to that reported during the five years before the interview. On the other hand, for the reporting period more than 20 years ago, there is a lower reported occurrence of miscarriage.

TABLE 22

MISCARRIAGE RATIOS BY AGE AT CONCEPTION AND YEAR OF CONCEPTION FOR NON-EXPOSED DEC FEMALE EMPLOYEES

AGE AT CONCEPTION	Year of Conception											
	BEFORE 1965			1965-1974			1975-1979			1980-1986		
	MISC	PREGS	RATIO	MISC	PREGS	RATIO	MISC	PREGS	RATIO	MISC	PREGS	RATIO
< 20	1	13	7.7	3	16	18.8	2	6	33.3	1	2	50.0
20-30	8	101	7.9	23	114	20.2	8	29	27.6	10	48	20.8
> 30	1	6	16.7	4	26	15.4	4	13	30.8	6	24	25.0

$$\text{Ratio} = (\text{MISC/PREGS}) \times 100 = (\text{No. Miscarriages/Total No. Pregnancies}) \times 100$$

In order to determine how this potential reporting decline could have affected the miscarriage ratio used for the non-exposed group, two strategies were employed. The first was to use only pregnancies reported after 1965 to estimate the non-exposed group miscarriage ratio (Table 23). The second approach involved calculating a "corrected" miscarriage ratio by adjusting the number of miscarriages in the period prior to 1965. Within each age stratum the total number of pregnancies prior to 1965 was inflated to maintain the post-1965 miscarriage ratio for that stratum. For example, among women less than 20 years of age at conception, there were 12 pregnancies prior to 1965 which resulted in either an induced abortion, stillbirth or livebirth. The algebraic expression of the miscarriage ratio with the number of pre-1965 miscarriages unknown  $\{x/(x + 12)\}$  was set equal to the post-1965 age-specific miscarriage ratio of 0.25 and the solution to x determined. The quantity x represents an estimate of the number of pre-1965 miscarriages if the post-1965 ratio is correct and is determined to be 4. Similarly, the estimate of the expected number of miscarriages in the other two age strata were calculated. The number of expected miscarriages prior to 1965 was estimated to be 32 which when combined with the 61 observed after 1965 yielded a total of 93 miscarriages for the

non-exposed group. The details of the derivation of these estimates are presented in Table 24, and an adjusted analysis is given in Table 25.

TABLE 23

RECALCULATION OF RELATIVE RISKS BASED ON POST-1965 CONCEPTIONS  
FOR THE NON-EXPOSED GROUP

EXPOSURE GROUP	MISCARRIAGE		OTHER THAN MISCARRIAGE	
	N	RATIO	N	RATIO
PHOTO	5	31.3	11	68.7
DIFFUSION	7	38.9	11	61.1
NON-EXPOSED	61	21.9	217	78.1

Relative risk of miscarriage comparing Photo to Non-exposed women = 1.34; 95% CIE = 0.62, 2.89.

Relative risk of miscarriage comparing Diffusion to Non-exposed women = 1.78; 95% CIE = 0.95, 3.30.

Relative risk of miscarriage comparing combined exposure groups (Photo + Diffusion) to Nonexposed women = 1.61; 95% CIE = (0.97, 2.67).

TABLE 24

ESTIMATED EXPECTED NUMBER OF MISCARRIAGES FOR NON-EXPOSED FEMALES  
IN THE PRE-1965 TIME PERIOD

AGE CATEGORY	POST 1965 MISCARRIAGE RATIO	PRE 1965 PREGNANCIES*	EXPECTED PRE 1965 MISCARRIAGES
< 20	25.0	12	4
20-30	21.5	93	26
> 31	22.2	5	2

\* Total number of induced abortions, stillbirths, and livebirths.

TABLE 25

RECALCULATION OF MISCARRIAGE RATIO AND RELATIVE RISKS BASED ON  
ESTIMATED PRE-1965 MISCARRIAGES AND OBSERVED  
POST-1965 MISCARRIAGES

EXPOSURE GROUP	MISCARRIAGE		OTHER THAN MISCARRIAGE	
	N	RATIO	N	RATIO
PHOTO	5	31.3	11	68.7
DIFFUSION	7	38.9	11	61.1
NON-EXPOSED	93	22.1	327	77.9

Relative risk of miscarriage comparing Photo to Non-exposed women = 1.41; 95% CIE = 0.67, 2.98.

Relative risk of miscarriage comparing Diffusion to Non-exposed women = 1.76; 95% CIE = 0.96, 3.22.

Relative risk of miscarriage comparing combined exposure groups (Photo + Diffusion) to Nonexposed women = 1.59; 95% CIE = (0.98, 2.60).

Using both inflated estimates of the Non-exposed miscarriage ratio resulted in the same general conclusion (Tables 23 and 25). The Photo and Diffusion group miscarriage ratios were still higher than in the Non-exposed group; the Diffusion comparison was of only borderline statistical significance, however. It should be clearly stated that the above analyses are not considered to be substitutes for the original results; they were conducted to help shed light on the potential recall bias.

One should also keep in mind the possibility that the lower reporting of miscarriage in the past reflects a truly lower incidence of this event. Given the increasing level of occupational and environmental exposures to new chemical and physical agents, one should not overlook the possibility that miscarriage has been an increasing phenomenon during the recent past.

With respect to external comparison populations, an attempt was made to gather data from the Massachusetts Department of Public Health about pregnancy outcomes in the region around Hudson. It was the investigators' opinion after reviewing the data, that these data were not suitable based on the collection and reporting mechanisms used.

General population surveys have usually reported miscarriage ratios in the 10-20% range (Table 26). (5-21) Cohort, cross-sectional, and case-control methodologies are included among these reports. Certainly, differences in selection criteria, populations studied, and methods of calculation will lead to

differing estimates. Furthermore, something analogous to the "infertile worker effect" may be operating for miscarriage.(2,22,23) If so, one would expect to find a higher proportion of women at risk of an adverse outcome in the workplace since these women are less likely to be absent from the workforce as a result of the birth of a child. These and other factors make the use of an internal comparison group preferable, in occupational studies.

TABLE 26

ESTIMATES OF THE SPONTANEOUS ABORTION (MISCARRIAGE) RATIO REPORTED  
IN THE LITERATURE

STUDY	MISCARRIAGE RATIO*	GESTATIONAL AGE CUTOFF (Weeks)
-----		
Cohort Study Design:		
French and Bierman (1962)	7.8	28
Erhardt (1963)	8.0	28
Pettersson (1968)	9.7	28
Taylor (1969)	3.6	28
Harlap et al. (1980)	4.8	28
Cross-sectional Study Design:		
Stevenson et al. (1959)	11.8	28
Shapiro et al. (1970)	14.3	28
Leridon (1976)	~11.5	Not Given
Case-Control Study Design:		
Yerushalmy et al. (1956)	5.7	20
Stevenson et al. (1959)	16.8	28
Warburton and Fraser (1964)	14.7	26
Jain (1969)	7.5	Term
Naylor (1974)	12.6	20
Leridon (1976) [Cretell]	15.3	Not Given
Leridon (1976) [Martinique]	12.1	Not Given

-----  
This table was taken from Bracken, M., Perinatal Epidemiology,  
Oxford University Press, 1984.(20)

\* The miscarriage ratio is also referred to as the fetal death ratio or spontaneous abortion ratio.

Another issue which should be addressed is the earlier gestational age at time of miscarriage among the Diffusion group.

One potential explanation is that there was selective recall of earlier adverse events within this group. Again, there is no explanation for why it would be manifest in this particular group, however. Another explanation is that some toxic effect may be acting early in pregnancy to cause fetal death. While such a biologic rationale needs to be tested in future studies, it should be noted that a recall bias in this case could, instead, result in an under-estimate of miscarriage risk. Specifically, since early miscarriages might be more subject to under-reporting, a risk measure associating some agent to early loss might result in a lower risk than actually exists if the risk is present.

The finding of a significantly increased risk of miscarriage among female Diffusion employees, and a non-significantly higher risk among female Photo employees, at the DEC Hudson facility when compared to an internal Non-exposed group needs to be considered in light of general medical knowledge about this reproductive outcome and also in light of the limitations of the present study.

Retrospective surveys of past pregnancies have contributed the largest amount of information known about population rates of spontaneous abortion. Known and purported causes of miscarriage include malformation, chromosomal abnormalities, gynecologic pathology, immunological factors, progesterone deficiency, infectious disease, IUD use, smoking and alcohol during pregnancy, maternal age and birth order, and chemicals and other environmental exposures.(1,24,25) While this study collected and analyzed information on most of these risk factors, it is difficult for any epidemiologic study to completely examine all possible risks in detail.

Miscarriage has been stated to be among the most useful outcomes for assessing occupational reproductive hazards.(26) The data reported here indicate a positive association between occupation in the fab area and risk for spontaneous abortion among females, beyond that which would be expected by chance. The observed rate of miscarriage of the Diffusion group was higher than in the comparison group and also higher than the level observed among these women prior to employment at the Hudson facility. This relation persisted even after controlling for a variety of risk factors for which data were available. The elevated risk among females in the Photo group, while not statistically significant, corresponds to a 31.3% occurrence of spontaneous abortion; this is higher than that which has been generally reported using comparable methodologies.

Studies to date have identified the testicular toxicity of acute glycol ether exposure in mice, rats, and rabbits.(27-34) Observed toxic effects include atrophy in size and weight of testes, and degeneration of germinal epithelium. Reversible

fertility loss has also been identified in these male species (30,35), as has teratogenicity (36-39). The nature and severity of events has varied depending on dose and route of administration. The fact that animal experiments indicate that a biological effect of glycol ether was to cause spontaneous abortion through its action on male gametes should not be viewed as an argument against a potential effect on the human female, since sufficient studies of females have not been conducted.

One study which examined male occupational exposure to ethylene glycol monomethyl ether at a Dow Chemical facility found a suggestion of smaller testicular size but no other gross or clinical differences in fertility indices.(40)

Finally, one needs in the future to better account for actual exposure levels encountered in the occupational setting. Only with more precise monitoring and data collection will exposure information be valuable enough to analyze in detail. With respect to glycol ethers, for example, Hudson Industrial hygiene monitoring data indicated levels well below industrial standards, or non-discernable levels, among persons in the fab areas. This should not be used to discount the present association, but should, instead, underscore the need to conduct more complete monitoring.

Most important, the results of this study should bear replication in future investigations using comparably exposed groups of workers. Given the context of this study, prompt attention to replication and validation of the findings should be initiated.

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**APPENDIX I:**

**Congenital Anomalies**

CONGENITAL ANOMALIES AMONG INFANTS OF DEC EMPLOYEES

EXPOSURE GROUP	REPORTED ANOMALY
Photo	Craniosynstosis
Photo	Hydrocele
Diffusion	Calcium deposits on skull
Nonexposed	High blood sugar; fluids in lungs
Nonexposed	Jaundice
Nonexposed	*Narrowing of aorta
Nonexposed	*Cerebral palsy
Nonexposed	*Cystic fibrosis
Nonexposed	*Situs inversus; immotil celcela syndrome
Nonexposed	*Down's syndrome
Nonexposed	*Slight mental retardation (birth trauma)
Nonexposed	*Pyloric stenosis
Nonexposed	*Hydrocephalus

\* Occurred prior to DEC employment.

**APPENDIX II:**

**Tables Of Individual Health Symptoms**

**SYMPTOM:**

- A. FREQUENT OR SEVERE SORE THROAT**
- B. ARTHRITIS**
- C. SLIPPED DISK**
- D. OTHER BACK PROBLEMS**
- E. FREQUENT OR SEVERE HEADACHES**
- F. FREQUENT OR SEVERE DIZZINESS**
- G. FREQUENT OR SEVERE NAUSEA**
- H. DIABETES**
- I. HIGH BLOOD PRESSURE**
- J. CANCER**
- K. THYROID DISORDERS**
- L. GALL BLADDER PROBLEMS**
- M. RESPIRATORY PROBLEMS**
- N. KIDNEY DISORDERS**
- O. SEIZURE DISORDERS**
- P. ANEMIA**
- Q. FREQUENT OR SEVERE RASH**
- R. FREQUENT OR SEVERE EYESTRAIN**

PREVALENCE RATIOS, CONFIDENCE INTERVAL ESTIMATES (95 % CIE), AND  
 PROBABILITIES ASSOCIATED WITH CHI SQUARE STATISTIC FOR GENERAL  
 HEALTH SYMPTOMS BY EXPOSURE GROUP AND SEX

SYMPTOM: FREQUENT OR SEVERE SORE THROATS

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b>BOTH SEXES:</b>					
PHOTO	12	123	2.64*	(1.27, 5.51)	0.011
DIFFUSION	14	144	2.64*	(1.30, 5.33)	0.008
COMBINED	26	267	2.64*	(1.42, 4.90)	0.002
NONEXPOSED **	15	431			
<b>MALES:</b>					
PHOTO	5	64	4.06	(0.81, 20.35)	0.146
DIFFUSION	6	85	3.69	(0.76, 17.86)	0.165
COMBINED	11	149	3.85	(0.87, 17.04)	0.099
NONEXPOSED	2	110			
<b>FEMALES:</b>					
PHOTO	7	59	2.73*	(1.13, 6.57)	0.029
DIFFUSION	8	59	3.07*	(1.32, 7.11)	0.010
COMBINED	15	118	2.90*	(1.42, 5.92)	0.004
NONEXPOSED	13	321			

\* Prevalence ratio significantly different from 1.0.

\*\* Referent group for calculating prevalence ratios for exposed groups.

SYMPTOM: ARTHRITIS

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	11	118	1.37	(0.70, 2.67)	0.262
DIFFUSION	9	148	0.92	(0.44, 1.91)	0.379
COMBINED	20	266	1.12	(0.64, 1.95)	0.368
NONEXPOSED	28	421			
<b><u>MALES:</u></b>					
PHOTO	1	65	0.34	(0.04, 2.87)	0.231
DIFFUSION	3	88	0.75	(0.18, 3.04)	0.366
COMBINED	4	153	0.58	(0.16, 2.10)	0.278
NONEXPOSED	5	108			
<b><u>FEMALES:</u></b>					
PHOTO	10	53	2.32*	(1.16, 4.63)	0.023
DIFFUSION	6	60	1.33	(0.56, 3.14)	0.323
COMBINED	16	113	1.81	(0.99, 3.32)	0.053
NONEXPOSED	23	313			

SYMPTOM: SLIPPED DISK

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	1	134	0.42	(0.05, 3.29)	0.274
DIFFUSION	3	154	1.07	(0.29, 3.98)	0.397
COMBINED	4	288	0.77	(0.23, 2.53)	0.363
NONEXPOSED	8	440			
<b><u>MALES:</u></b>					
PHOTO	0	68	1.64	(0.03, 81.60)	0.387
DIFFUSION	3	88	8.60	(0.45, 164.34)	0.089
COMBINED	3	156	4.94	(0.26, 94.78)	0.198
NONEXPOSED	0	112			
<b><u>FEMALES:</u></b>					
PHOTO	1	66	0.63	(0.08, 4.93)	0.361
DIFFUSION	0	66	0.30	(0.02, 5.07)	0.266
COMBINED	1	132	0.32	(0.04, 2.50)	0.204
NONEXPOSED	8	328			

SYMPTOM: OTHER BACK PROBLEMS

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	23	112	0.91	(0.59, 1.37)	0.350
DIFFUSION	21	136	0.71	(0.45, 1.10)	0.113
COMBINED	44	248	0.79	(0.57, 1.11)	0.157
NONEXPOSED	85	363			
<b><u>MALES:</u></b>					
PHOTO	12	56	1.52	(0.74, 3.14)	0.209
DIFFUSION	15	76	1.42	(0.71, 2.83)	0.242
COMBINED	27	132	1.46	(0.79, 2.71)	0.188
NONEXPOSED	13	99			
<b><u>FEMALES:</u></b>					
PHOTO	11	56	0.77	(0.43, 1.37)	0.250
DIFFUSION	6	60	0.42*	(0.19, 0.94)	0.027
COMBINED	17	116	0.60*	(0.37, 0.97)	0.039
NONEXPOSED	72	264			

SYMPTOM: FREQUENT OR SEVERE HEADACHES

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	30	106	1.05	(0.73, 1.52)	0.383
DIFFUSION	48	109	1.46*	(1.09, 1.96)	0.020
COMBINED	78	215	1.27	(0.98, 1.65)	0.073
NONEXPOSED	94	355			
<b><u>MALES:</u></b>					
PHOTO	11	58	0.86	(0.44, 1.67)	0.359
DIFFUSION	17	74	1.01	(0.57, 1.79)	0.399
COMBINED	28	132	0.94	(0.56, 1.57)	0.389
NONEXPOSED	21	92			
<b><u>FEMALES:</u></b>					
PHOTO	19	48	1.31	(0.85, 2.01)	0.199
DIFFUSION	31	35	2.16*	(1.56, 3.00)	<0.001
COMBINED	50	83	1.73*	(1.28, 2.33)	<0.001
NONEXPOSED	73	263			

SYMPTOM: FREQUENT OR SEVERE DIZZINESS

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	9	127	2.12	(0.94, 4.80)	0.074
DIFFUSION	6	152	1.22	(0.48, 3.12)	0.366
COMBINED	15	279	1.64	(0.80, 3.34)	0.048
NONEXPOSED	14	435			
<b><u>MALES:</u></b>					
PHOTO	3	66	11.40	(0.60, 217.43)	0.102
DIFFUSION	4	87	11.15	(0.61, 204.48)	0.081
COMBINED	7	153	10.62	(0.61, 184.11)	0.062
NONEXPOSED	0	113			
<b><u>FEMALES:</u></b>					
PHOTO	6	61	2.15	(0.86, 5.39)	0.180
DIFFUSION	2	65	0.72	(0.17, 3.08)	0.361
COMBINED	8	126	1.43	(0.62, 3.34)	0.281
NONEXPOSED	14	322			

SYMPTOM: FREQUENT OR SEVERE NAUSEA

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	10	124	2.55*	(1.14, 5.68)	0.025
DIFFUSION	13	142	2.87*	(1.36, 6.04)	0.006
COMBINED	23	266	2.72*	(1.40, 5.28)	0.003
NONEXPOSED	13	431			
<b><u>MALES:</u></b>					
PHOTO	3	65	4.90	(0.52, 46.14)	0.121
DIFFUSION	7	82	8.73*	(1.09, 69.65)	0.018
COMBINED	10	147	7.07	(0.92, 54.44)	0.056
NONEXPOSED	1	110			
<b><u>FEMALES:</u></b>					
PHOTO	7	59	2.94*	(1.20, 7.20)	0.033
DIFFUSION	6	60	2.52	(0.98, 6.48)	0.102
COMBINED	13	119	2.73*	(1.28, 5.83)	0.011
NONEXPOSED	12	321			

SYMPTOM: DIABETES

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	3	133	4.96	(0.84, 29.40)	0.154
DIFFUSION	1	156	1.43	(0.13, 15.70)	0.257
COMBINED	4	289	3.07	(0.57, 16.66)	0.156
NONEXPOSED	2	448			
<b><u>MALES:</u></b>					
PHOTO	0	69	DUE TO SMALL NUMBER OF CASES, NO ANALYSES DONE		
DIFFUSION	1	90			
COMBINED	1	159			
NONEXPOSED	0	113			
<b><u>FEMALES:</u></b>					
PHOTO	3	64	7.55*	(1.29, 44.29)	0.013
DIFFUSION	0	66	1.01	(0.05, 20.78)	0.398
COMBINED	3	130	3.80	(0.64, 22.49)	0.114
NONEXPOSED	2	335			

SYMPTOM: HIGH BLOOD PRESSURE

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	12	124	1.17	(0.62, 2.19)	0.356
DIFFUSION	14	142	1.19	(0.65, 2.15)	0.342
COMBINED	26	266	1.18	(0.72, 1.92)	0.323
NONEXPOSED	34	415			
<b><u>MALES:</u></b>					
PHOTO	4	65	0.73	(0.23, 2.27)	0.343
DIFFUSION	7	82	0.99	(0.38, 2.55)	0.399
COMBINED	11	147	0.87	(0.38, 2.04)	0.379
NONEXPOSED	9	104			
<b><u>FEMALES:</u></b>					
PHOTO	8	59	1.61	(0.76, 3.40)	0.188
DIFFUSION	7	60	1.40	(0.63, 3.11)	0.283
COMBINED	15	119	1.50	(0.82, 2.76)	0.168
NONEXPOSED	25	311			

SYMPTOM: CANCER

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b>BOTH SEXES:</b>					
<u>PHOTO</u>	0	135	0.26	(0.01, 4.49)	0.238
DIFFUSION	2	156	0.95	(0.19, 4.65)	0.399
COMBINED	2	291	0.51	(0.10, 2.51)	0.280
NONEXPOSED	6	443			
<b>MALES:</b>					
<u>PHOTO</u>	0	69	DUE TO SMALL NUMBER OF CASES, NO ANALYSES DONE		
DIFFUSION	1	90			
COMBINED	1	159			
NONEXPOSED	0	113			
<b>FEMALES:</b>					
<u>PHOTO</u>	0	66	0.39	(0.02, 6.79)	0.317
DIFFUSION	1	66	0.84	(0.10, 6.83)	0.393
COMBINED	1	132	0.42	(0.05, 3.46)	0.283
NONEXPOSED	6	330			

SYMPTOM: THYROID DISORDERS

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	4	132	2.20	(0.63, 7.67)	0.180
DIFFUSION	1	156	0.48	(0.06, 3.92)	0.311
COMBINED	5	288	1.27	(0.39, 4.14)	0.368
NONEXPOSED	6	442			
<b><u>MALES:</u></b>					
PHOTO	0	69	DUE TO SMALL NUMBER OF CASES, NO ANALYSES DONE		
DIFFUSION	1	90			
COMBINED	1	159			
NONEXPOSED	0	112			
<b><u>FEMALES:</u></b>					
PHOTO	4	63	3.34	(0.97, 11.53)	0.114
DIFFUSION	0	66	0.39	(0.02, 6.79)	0.317
COMBINED	4	129	1.68	(0.48, 5.87)	0.284
NONEXPOSED	6	330			

SYMPTOM: GALL BLADDER PROBLEMS

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	2	134	1.09	(0.22, 5.35)	0.397
DIFFUSION	2	156	0.94	(0.19, 4.61)	0.398
COMBINED	4	290	1.01	(0.29, 3.55)	0.399
NONEXPOSED	6	440			
<b><u>MALES:</u></b>					
PHOTO	0	69	DUE TO THE LACK OF CASES, NO ANALYSES DONE		
DIFFUSION	0	91			
COMBINED	0	160			
NONEXPOSED	0	111			
<b><u>FEMALES:</u></b>					
PHOTO	2	65	1.67	(0.34, 8.08)	0.325
DIFFUSION	2	65	1.67	(0.34, 8.08)	0.325
COMBINED	4	130	1.67	(0.48, 5.81)	0.288
NONEXPOSED	6	329			

SYMPTOM: RESPIRATORY PROBLEMS

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	17	115	1.35	(0.79, 2.28)	0.219
DIFFUSION	14	142	0.94	(0.53, 1.67)	0.389
COMBINED	31	257	1.13	(0.73, 1.75)	0.347
NONEXPOSED	42	397			
<b><u>MALES:</u></b>					
PHOTO	6	60	1.21	(0.44, 3.32)	0.374
DIFFUSION	6	84	0.88	(0.32, 2.45)	0.387
COMBINED	12	144	1.02	(0.43, 2.41)	0.399
NONEXPOSED	8	98			
<b><u>FEMALES:</u></b>					
PHOTO	11	55	1.63	(0.87, 3.05)	0.127
DIFFUSION	8	58	1.19	(0.58, 2.45)	0.359
COMBINED	19	113	1.41	(0.84, 2.38)	0.177
NONEXPOSED	34	299			

**SYMPTOM: KIDNEY DISORDERS**

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	2	133	0.44	(0.10, 1.91)	0.210
DIFFUSION	2	155	0.38	(0.09, 1.65)	0.160
COMBINED	4	288	0.41	(0.14, 1.22)	0.099
NONEXPOSED	15	433			
<b><u>MALES:</u></b>					
PHOTO	1	67	0.82	(0.08, 8.91)	0.393
DIFFUSION	0	90	0.25	(0.01, 5.11)	0.247
COMBINED	1	157	0.35	(0.03, 3.86)	0.269
NONEXPOSED	2	110			
<b><u>FEMALES:</u></b>					
PHOTO	1	66	0.39	(0.05, 2.90)	0.249
DIFFUSION	2	65	0.77	(0.18, 3.34)	0.376
COMBINED	3	131	0.58	(0.17, 2.00)	0.271
NONEXPOSED	13	323			

SYMPTOM: SEIZURE DISORDERS

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	1	134	1.66	(0.15, 18.16)	0.374
DIFFUSION	1	156	1.43	(0.13, 15.63)	0.381
COMBINED	2	290	1.53	(0.22, 10.83)	0.363
NONEXPOSED	2	446			
<b><u>MALES:</u></b>					
PHOTO	0	68	DUE TO LACK OF CASES, NO ANALYSES DONE		
DIFFUSION	0	91			
COMBINED	0	159			
NONEXPOSED	0	112			
<b><u>FEMALES:</u></b>					
PHOTO	1	66	2.51	(0.23, 27.26)	0.294
DIFFUSION	1	65	2.55	(0.23, 27.67)	0.291
COMBINED	2	131	2.53	(0.36, 17.75)	0.251
NONEXPOSED	2	334			

SYMPTOM: ANEMIA

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b>BOTH SEXES:</b>					
PHOTO	10	125	0.92	(0.45, 1.80)	0.387
DIFFUSION	8	148	0.64	(0.30, 1.34)	0.190
COMBINED	18	273	0.77	(0.44, 1.32)	0.252
NONEXPOSED	36	410			
<b>MALES:</b>					
PHOTO	2	66	8.26	(0.40, 169.56)	0.103
DIFFUSION	2	88	6.26	(0.30, 128.85)	0.155
COMBINED	4	154	6.45	(0.35, 118.68)	0.139
NONEXPOSED	0	113			
<b>FEMALES:</b>					
PHOTO	8	59	1.10	(0.54, 2.27)	0.385
DIFFUSION	6	60	0.84	(0.37, 1.92)	0.366
COMBINED	14	119	0.97	(0.54, 1.75)	0.397
NONEXPOSED	36	297			

SYMPTOM: FREQUENT OR SEVERE RASH

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % C I E (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	11	125	1.58	(0.79, 3.16)	0.172
DIFFUSION	13	144	1.62	(0.84, 3.11)	0.141
COMBINED	24	269	1.60	(0.92, 2.78)	0.098
NONEXPOSED	23	426			
<b><u>MALES:</u></b>					
PHOTO	2	67	0.82	(0.15, 4.35)	0.387
DIFFUSION	9	82	2.79	(0.89, 8.78)	0.073
COMBINED	11	149	1.94	(0.63, 5.95)	0.196
NONEXPOSED	4	109			
<b><u>FEMALES:</u></b>					
PHOTO	9	58	2.38*	(1.12, 5.02)	0.029
DIFFUSION	4	62	1.07	(0.38, 3.05)	0.395
COMBINED	13	120	1.73	(0.88, 3.40)	0.112
NONEXPOSED	19	317			

SYMPTOM: FREQUENT OR SEVERE EYESTRAIN

	TOTAL WITH SYMPTOMS	TOTAL WITHOUT SYMPTOMS	PREVALENCE RATIO	95 % CIE (LL, UL)	P-VALUE
<b><u>BOTH SEXES:</u></b>					
PHOTO	30	106	1.02	(0.71, 1.47)	0.397
DIFFUSION	33	125	0.97	(0.68, 1.38)	0.393
COMBINED	63	231	0.99	(0.75, 1.32)	0.399
NONEXPOSED	96	349			
<b><u>MALES:</u></b>					
PHOTO	12	57	0.72	(0.39, 1.33)	0.226
DIFFUSION	16	75	0.73	(0.42, 1.27)	0.210
COMBINED	28	132	0.73	(0.45, 1.16)	0.164
NONEXPOSED	27	85			
<b><u>FEMALES:</u></b>					
PHOTO	18	49	1.30	(0.83, 2.03)	0.215
DIFFUSION	17	50	1.23	(0.77, 1.94)	0.278
COMBINED	35	99	1.26	(0.89, 1.80)	0.178
NONEXPOSED	69	264			

**APPENDIX III:**

- A. Informed Consent Form**
- B. Main Interview Form**
- C. Female Reproductive Questionnaire**
- D. Male Reproductive Questionnaire**



UNIVERSITY OF MASSACHUSETTS  
AT AMHERST

School of Health Sciences  
Division of Public Health

Arnold House — Morrill Science Center  
Amherst, MA 01003

I give my permission to the University of Massachusetts Division of Public Health (UMDPH) study team to contact my spouse/doctor/hospital for further specific health information, if necessary. I understand the contact with my spouse would be a brief one-time, telephone interview involving questions about general health and pregnancy histories. I also understand contact with my doctor or hospital will involve the verification of specific medical questions which I responded to during the interview, for example, the specific name of an illness or medication.

\_\_\_\_\_  
Signature of Participant

\_\_\_\_\_  
Date

Name of Participant: \_\_\_\_\_  
(last) (first)

Study ID Number: \_\_\_\_\_

Spouse's Name: \_\_\_\_\_

Spouse's Telephone Number: \_\_\_\_\_ - \_\_\_\_\_

Convenient time to call: \_\_\_\_\_ : \_\_\_\_\_ a.m./p.m.

Doctor: \_\_\_\_\_

Hospital: \_\_\_\_\_

Address: \_\_\_\_\_

Address: \_\_\_\_\_

Doctor: \_\_\_\_\_

Hospital: \_\_\_\_\_

Address: \_\_\_\_\_

Address: \_\_\_\_\_

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UNIVERSITY OF MASSACHUSETTS  
AT AMHERST

School of Health Sciences  
Division of Public Health

Arnold House — Morrill Science Center  
Amherst, MA 01003

Your cooperation is being requested for a general health study of manufacturing and non-manufacturing personnel at the Hudson facility. The study is being sponsored by D.E.C. and being conducted by the University of Massachusetts Division of Public Health (UMDPH).

We would like to interview you for about 30 minutes to ask about basic background information such as age, height, weight, a general health and reproductive history, a general life style history, and present and past occupational history. Based on your responses during the questionnaire, we may also ask your permission to contact your spouse, doctor or hospital for further specific health information. At the conclusion of this interview, you will be given the opportunity to provide this permission on a separate form.

You have the option to participate, not participate or to participate but not answer certain questions in the interview. The time you spend during the interview will be treated as part of your normal workday and will be paid as such.

Any responses you give will be held in strict confidence and will be seen and used only by the UMDPH study team. Information will be released to D.E.C. in the form of summary statistics which will not include the names or badge numbers of individuals or other identifying information. A summary of results will be made available to you by D.E.C. at the conclusion of the study.

-----

I have been told that my participation is voluntary and will in no way affect my job or my relationship with D.E.C. The interviewer has answered all of my questions and I may refer any future questions about the study to:

Dr. Edward Calabrese at (413) 545-2797 or  
Dr. Harris Pastides at (413) 545-0432

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of Participant

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MAIN INTERVIEW  
(Completed by each  
participant)

Study ID Number: \_\_\_\_

Date of Interview: \_\_/\_\_/\_\_

Interviewer Code: \_

Starting Time: \_\_:\_\_

Ending Time: \_\_:\_\_

TOTAL TIME: \_\_:\_\_

.....

Sex: \_\_ 1=male 2=female (do not ask)

First I would like to ask you some background questions. . . .

What is your date of birth? \_\_/\_\_/\_\_

Are you currently married, divorced, separated, widowed, or have you never been married? \_\_ 1=currently married  
2=currently divorced  
3=currently separated  
4=currently widowed  
5=never married

What is your current height? \_\_ feet \_\_ inches

What is your current weight? \_\_ pounds

What was the highest grade of school you completed? \_\_

<u>Grade school</u>								<u>High School</u>				<u>College or Vocational</u>				<u>Professional or Graduate School</u>				
1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	1	2	3	4	+
												(13,14,15,16)				(17,18,19,20)				

What is your ethnic group? \_\_\_\_\_

What is your religion? \_\_\_\_\_

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Now, I would like to ask you about your employment history. . .

What month and year did you begin work at the Hudson  
City of 2000 / /  
mo yr

0.1 Would you tell me the first/second, etc. cost center or the cost center code in which you were located?

0.2 What was/is your job title and job code?

0.3 Could you please give me the beginning and ending dates of your employment in this position?

	1st position held	2nd position held	3rd position held	4th position held
COST CENTER	-----	-----	-----	-----
JOB CODE	-----	-----	-----	-----
JOB TITLE	-----	-----	-----	-----
LENGTH OF POSITION	from ___/___ to ___/___	from ___/___ to ___/___	from ___/___ to ___/___	from ___/___ to ___/___

IF MORE ROOM NECESSARY, INSERT EXTRA SHEET

.....  
IF COST CENTER IS Custom or Interim THEN FOLLOW JOB TITLE TO ANALOGOUS PAGE (4PM, 4PS, 4PV, 4PX, 4QL, 4QQ, 4QR)

- manager/supervisor ==> page 3
- engineer ==> page 4
- technician ==> page 5
- operator/work coordinator/inspector ==> page 7
- other non-clerical, non-secretarial positions ==> page 5
- clerical, secretarial positions skip to page 13

ALL OTHER COST CENTERS SKIP TO PAGE 13

MANAGER/SUPERVISOR

	1st pos. held	2nd pos. held	3rd pos. held	4th pos. held
On average, how many hours per week do/did you spend in the fab area?	-----	-----	-----	-----
Do/Did you ever spend any time in the fab area instructing workers on chemical handling techniques, repairing or cleaning machines, or other procedures? 0=No 1=Yes	-----	-----	-----	-----
If yes: Do/Did you personally use chemicals while instructing workers? 0=No 1=Yes	-----	-----	-----	-----
If yes: What is/was the most number of hours per day you would spend using chemicals?	-----	-----	-----	-----
Would you say you would do this at least once a week? 0=No 1=Yes	-----	-----	-----	-----

.....  
 GO TO PAGE 8 FOR GENERAL WORK PRACTICE QUESTIONS  
 .....

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PAGE 4

**ENGINEER**

	1st pos. held -----	2nd pos. held -----	3rd pos. held -----	4th pos. held -----
--	---------------------------	---------------------------	---------------------------	---------------------------

On average, how many hours per day do/did you spend in the sub area?

	-----	-----	-----	-----
--	-------	-------	-------	-------

Referring to the map, could you tell me the chemical use stations where you work/worked and the percentage of time you spend/spent there per day, listing them in the order of most-time spent to least-time spent:

- 1=0 to 20 %
- 2=21 to 40 %
- 3=41 to 60 %
- 4=61 to 80 %
- 5=81 to 100%

	---	---	---	---
station with most-time				
% of time				
-----				
station				
% of time				
-----				
station				
% of time				
-----				
station				
% of time				
-----				
station with least-time				
% of time				
-----				

Do/Did you use any chemicals while in the fab area? 0=No 1=Yes

If yes: What is/was the most number of hours per day you would spend using chemicals?

Would you say you would do this at least once a week? 0=No 1=Yes

GO TO PAGE 8 FOR GENERAL WORK PRACTICE QUESTIONS

TECHNICIAN

1st pos. held	2nd pos. held	3rd pos. held	4th pos. held
-----	-----	-----	-----

Do/Did you perform the duties of a manufacturing, a repair and maintenance (R & M), a production or other type of technician?

- 1=manufacturing
- 2=R & M
- 3=production
- 4=other

On average, how many hours per day do/did you spend in the fab area?

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PAGE 6

Referring to the map, could you tell me the chemical use stations where you work/worked and the percentage of time you spend/spent there per day, listing them in the order of most-time spent to least-time spent?

- 1=0 to 20 %
- 2=21 to 40 %
- 3=41 to 60 %
- 4=61 to 80 %
- 5=81 to 100%

	1st pos. held	2nd pos. held	3rd pos. held	4th pos. held
	-----	-----	-----	-----
station with most-time	--	--	--	--
% of time	--	--	--	--
-----				
station	--	--	--	--
% of time	--	--	--	--
-----				
station	--	--	--	--
% of time	--	--	--	--
-----				
station	--	--	--	--
% of time	--	--	--	--
-----				
station with least-time	--	--	--	--
% of time	--	--	--	--
-----				

.....  
 GO TO PAGE 8 FOR GENERAL WORK PRACTICE QUESTIONS  
 .....

OPERATOR/INSPECTOR/WORK COORDINATOR

	1st pos. held	2nd pos. held	3rd pos. held	4th pos. held
--	------------------	------------------	------------------	------------------

How many hours per day do/did you spend in the fab area?

Referring to the map, could you show me the station(s) at which you have/had ever work/worked, the number of months you work/worked at the station (this includes training time), and the percentage time you spend/spent there per day?

- 1=0 to 20 %
- 2=21 to 40 %
- 3=41 to 60 %
- 4=61 to 80 %
- 5=81 to 100%

station				
# months				
% time				
station				
# months				
% time				
station				
# months				
% time				
station				
# months				
% time				
station				
# months				
% time				

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GENERAL WORK PRACTICE

	1st pos. held	2nd pos. held	3rd pos. held	4th he
	-----	-----	-----	-----
Do/did you regularly use any chemical protective gear?				
0=No 1=yes				
1=yes: Which of the following do/did you use when working with chemicals? . . . Do/Did you use . . .				
0=No 1=yes?				
Which types . . .				
orange/yellow(acid)?				
green/blue(solvent)				
ivory/white(nylon)?				
clear (PVC)?				
Arm guards?				
Face shield?				
Gloves?				
Respirator (SCBA)?				
Safety glasses?				
Protective suit?(Tyvek)				
Chem. resistant boots				
Do/Did you do any chemical handling or mixing?				
0=No 1=yes				
1=yes: Could you tell me how much of your time per day is/was spent performing this activity?				
1=0 to 20 %				
2=21 to 40 %				
3=41 to 60 %				
4=61 to 80 %				
5=81 to 100%				

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1st pos. held	2nd pos. held	3rd pos. held	4th pos. held
-----	-----	-----	-----

Please tell me the number of all the following substances that you handle/handled or mix/mixed? (show card)

-----  
-----  
-----

Are there any other chemicals not listed here, which you believe you had contact with?

-----  
-----  
-----

... Do/Did you do any cleaning of equipment or machines?

0=No 1=yes

If yes: Could you tell me how much of your time per day is/was spent performing this activity?

- 1=0 to 20 %
- 2=21 to 40 %
- 3=41 to 60 %
- 4=61 to 80 %
- 5=81 to 100%

Do/did you wear any protective equipment?

0=No 1=yes

If yes: What do/did you use? . . .

Gloves?

If yes: Which types. . .

- orange/yellow(acid)?
- green/blue(solvent)?
- ivory/white(nylon)?
- clear(PVC)?

Arm guards?

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	1st pos. held	2nd pos. held	3rd pos. held	4th pos. held
Face shield?				
Apron				
Respirator (SCBA)?				
Safety glasses				
Protective suit? (Tyvek)				
Chem. resistant boots				

Did you do any repairing of equipment or machines?  
 1=No 2=Yes

If yes: Could you tell me how much of your time per day is/was spent performing this activity?

- 1=0 to 20 %
- 2=21 to 40 %
- 3=41 to 60 %
- 4=61 to 80 %
- 5=81 to 100%

Did you wear any protective equipment?  
 0=No 1=Yes

If yes: What did you use? . . .

Gloves?

If yes: Which types. . .

- orange/yellow (acid)?
- green/blue (solvent)?
- ivory/white (nitril)?
- clear (PVC)?

Arm guards?

Face shield?

Apron?

Respirator (SCBA)?

Safety glasses?

Protective suit? (Tyvek)

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Page 2

1st pos.  
held

2nd pos.  
held

3rd pos.  
held

4th pos.  
held

Were/Are you ever involved  
in chemical spill clean-ups?

If yes: Could you tell  
me how much of your time  
per day is/was spent  
performing this activity?

1=0 to 20 %

2=21 to 40 %

3=41 to 60 %

4=61 to 80 %

5=81 to 100%

How many times per month  
do/did you clean up acid  
spills?

Do/did you wear any  
protective equipment  
during the spill clean-up?

0=No 1=yes

If yes: What do/did  
you use?

Gloves?

If yes: Which types?  
orange/yellow (acid)?  
green/blue (solvent)?  
ivory/white (nylon)?  
clear (PVC)?

Arm guards?

Face shield?

Apron?

Respirator (SCBA)?

Safety glasses?

Protective suit (Tyvek)?

Other assistance?

How many times per month  
do/did you clean up  
solvent spills?

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PAGE 12

	1st pos. held	2nd pos. held	3rd pos. held	4th held
<p>do/did you wear any protective equipment during the spill clean-up? 0=No 1=yes</p> <p>If yes: What do/did you use? . . .</p> <p>Gloves?</p> <p>If yes: Which types. . .</p> <p style="padding-left: 40px;">orange/yellow(acid)?</p> <p style="padding-left: 40px;">green/blue(solvent)?</p> <p style="padding-left: 40px;">ivory/white(nylon)?</p> <p style="padding-left: 40px;">clear(PVC)?</p> <p>Arm guards?</p> <p>Face shield?</p> <p>Apron?</p> <p>Respirator(SCBA)?</p> <p>Safety glasses?</p> <p>Have you been trained in proper spill clean-up techniques? 0=No 1=yes</p> <p>On average, how many hours of overtime did you put in per week while in this position?</p> <p>If yes: What percentage of overtime is spent in the fab area? 1=0 to 20 % 2=21 to 40 % 3=41 to 60 % 4=61 to 80 % 5=81 to 100%</p>	-	-	-	-

.....  
DID YOU HOLD ANY OTHER POSITIONS WITHIN THIS COST CENTER?

IF YES ==> RETURN TO Q.2, PAGE 2

IF NO ==> DID YOU HOLD ANY OTHER POSITIONS IN OTHER COST CENTERS?

IF YES ==> RETURN TO Q.1, PAGE 2

IF NO ==> GO TO NEXT SECTION

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The next questions I would like to ask you are about your general health.

During the past 5 years have you had any of the following medical conditions?

Diabetes?  0=No 1=Yes 2=Unsure

If yes: How long have you had diabetes?  years

High blood pressure?  0=No 1=Yes 2=Unsure

If yes: How long have you had high blood pressure?  years  
What medication do you take for this?

Cancer?  0=No 1=Yes 2=Unsure

If yes: What type of cancer did you have?

When was your cancer first diagnosed?

\*\*Did you receive any radiation treatment or chemotherapy?  0=No 1=Yes 2=Unsure

Thyroid Problems?  0=No 1=Yes 2=Unsure

If yes: \*\*Is it an over-active thyroid problem or an under-active one?  1=Over-active  
2=Under-active

Gallbladder problems?  0=No 1=Yes 2=Unsure

Respiratory problems such as asthma, chronic bronchitis, or pneumonia?  0=No 1=Yes 2=Unsure

If yes: Did you have asthma?  How long?  years

Did you have chronic bronchitis?  How long?  years

Did you have pneumonia?

Kidney disorders?  0=No 1=Yes 2=Unsure

If yes: How long have you had a kidney disorder?  years

Convulsive disorders or seizures?  0=No 1=Yes 2=Unsure

If yes: How long did you have a convulsive disorder or seizure?  years

Arthritis?  0=No 1=Yes 2=Unsure

If yes: How long have you had arthritis?  years

Anemia or low blood count?  0=No 1=Yes 2=Unsure

If yes: How long were you anemic?  months

Slipped disc?  0=No 1=Yes 2=Unsure

PAGE 14

Other back problems? \_ 0=No 1=Yes 2=Unsure

If yes: What kind of back problem do/did you have? \_\_\_\_\_  
\_\_\_\_\_

How long have you had this back problem? \_\_\_ years

Frequent sore throats? \_ (frequent means more than 2 per month)

If yes: How long have you had these? \_\_\_ years  
On average, how many times per month? \_\_\_

Frequent or severe headaches? \_ 0=No 1=Yes (frequent means more  
2=Unsure than 3 per mo

If yes: In total, how many months did these headaches occur? \_\_\_  
On average, how many did you have per month? \_\_\_

Frequent or severe rashes? \_ 0=No 1=Yes (frequent means more tha  
2=Unsure 2 per month)

If yes: In total, how many months did these rashes occur? \_\_\_  
On average, how many did you have per month? \_\_\_

Frequent or severe dizziness? \_ 0=No 1=Yes 2=Unsure

If yes: How many months did this condition last? \_\_\_ months  
How many times per month did you have dizziness? \_\_\_

Frequent or severe eye strain? \_ 0=No 1=Yes 2=Unsure

If yes: How many months did this condition last? \_\_\_ months  
How many times per month did you have eye strain? \_\_\_

Frequent or severe nausea? \_ 0=No 1=Yes 2=Unsure

If yes: How many months did this condition last? \_\_\_ months  
How many times per month did you feel nauseous? \_\_\_

**If male: GO TO TOP OF NEXT PAGE**

**If female: CONTINUE BELOW**

Have you ever been vaccinated for rubella (German measles)? \_ 0=No 1=Yes  
2=Unsure

If yes: In what year did you have a vaccination? 19\_\_

Have you ever had mammography, or x-rays of the breast? \_ 0=No 1=Yes  
2=Unsure

If yes: How many times? \_\_\_

Have you ever had cysts or lumps of the breast? \_ 0=No 1=Yes 2=Unsure

If yes: Was a biopsy or surgical removal performed? \_ 0=No 1=Yes  
2=Unsure

How many times did you have such a condition? \_\_\_

Have you ever had any gynecological problems such as  
\_\_\_\_\_ 0=No 1=Yes 2=Unsure

Did you have any birth defects when you were born?  0=No  1=Yes  2=Unsure

If yes: What were they? \_\_\_\_\_

Did anyone in your immediate family (this includes parents, brothers and sisters) have any birth defects?  0=No  1=Yes  2=Unsure

If yes: Which family member had a birth defect?  1=Father  2=Mother  3=Brother  4=Other

What was the birth defect? \_\_\_\_\_

Have you ever taken any of the following medications?

Insulin?  0=No  1=Yes  2=Unsure

If yes: For how long have you taken insulin? \_\_\_\_\_ years

Medication for high BP?  0=No  1=Yes  2=Unsure

If yes: What are the medications? \_\_\_\_\_

How long did you take \_\_\_\_\_

How long did you take \_\_\_\_\_

Did your mother take DES?  0=No  1=Yes  2=Unsure

\*\*If yes: Did she take DES during the pregnancy when she had you?  0=No  1=Yes  2=Unsure

Vitamins?  0=No  1=Yes  2=Unsure

If yes: How long did you take vitamins? \_\_\_\_\_ years

Aspirin?  0=No  1=Yes  2=Unsure

If yes: How many aspirin pills do you take per month? \_\_\_\_\_

If female:

DES?  0=No  1=Yes  2=Unsure

If yes: How long did you take DES? \_\_\_\_\_ months

Now, I would like to ask some questions about your home, your diet and certain activities. . .

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PAGE 16

If yes: How many times a year do you have your lawn sprayed? \_\_\_

Do you use any of the following cleaning fluids in your home. . .

. . . floor cleaners? \_\_\_

0=No 1=Yes 2=Unsu

About how many times per month do you use this? \_\_\_

. . . wax strippers? \_\_\_

0=No 1=Yes 2=Unsu

About how many times per month do you use this? \_\_\_

. . . furniture refinishers? \_\_\_

0=No 1=Yes 2=Unsu

About how many times per year do you use this? \_\_\_

Do you use pesticides/herbicides on your garden, shrubs or plants? \_\_\_

0=No 1=Yes 2=Unsu

If yes: About how many times per year? \_\_\_

Has your house ever been treated by you or a professional with a chemical for termites? \_\_\_

0=No 1=Yes 2=Unsu

If yes: When was this done? \_\_\_/\_\_\_

Do you have hobbies in which you regularly use any of the following:

- paint? \_\_\_

0=No 1=Yes 2=Unsu

- varnish? \_\_\_

0=No 1=Yes 2=Unsu

- adhesives or glues? \_\_\_

0=No 1=Yes 2=Unsu

- solvents? \_\_\_

0=No 1=Yes 2=Unsu

- paint stripper? \_\_\_

0=No 1=Yes 2=Unsu

- degreasers? \_\_\_

0=No 1=Yes 2=Unsu

- lead? \_\_\_

0=No 1=Yes 2=Unsu

Did you/your husband serve in the armed forces and have any exposure to the chemical agent orange? \_\_\_

0=No 1=Yes 2=Unsu

Do you use artificial sweeteners, such as saccharin? \_\_\_

0=No 1=Yes 2=Unsu

If yes: How many times per week do you use them? \_\_\_

0=No 1=Yes 2=Unsu

Do you drink soft drinks containing artificial sweeteners? \_\_\_

0=No 1=Yes 2=Unsu

If yes, how many do you drink per week? \_\_\_

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Do you now or did you ever drink coffee, tea or soft drinks containing caffeine on a regular basis?

0=No 1=Yes 2=Unsure

If yes: On average, how many cups or glasses do you drink per day of. . .

Caffeinated Coffee	Caffeinated Hot tea	Caffeinated Cold tea	Soft drinks containing caffeine
-----	-----	-----	-----
---	---	---	---

Is your present overall caffeine consumption greater, less or about the same as 5 years ago?

1=greater  
2=less  
3=same

Have you ever smoked at least 1 cigarette a day for as much as 3 months?

0=No 1=Yes 2=Unsure

If yes:

At what age did you begin smoking?

In total, for how many years have you smoked?

On average, how many packs per day do/did you smoke?

Do/did you usually smoke low-tar cigarettes, another type of filtered cigarette or unfiltered cigarettes?

1=Low-tar  
2=Another type of filtered cigarette  
3=Unfiltered cigarette

Do/did you usually inhale into the chest, into the throat or do not inhale at all?

1=Chest  
2=Throat  
3=Not at all

Do you now or did you ever drink any kind of alcoholic beverage (this includes wine, beer, or distilled spirits)?

0=No 1=Yes 2=Unsure

If yes: Which of the following do you occasionally or regularly consume?

Wine	Beer	Spirits (ie. bourbon, gin, rye, scotch, vodka, etc.)
-----	-----	-----
---	---	---

0=No 1=Yes  
2=Unsure

Amount	Wine glasses per week	Beer bottles/cans per week	Spirits (ie. bourbon, gin, rye, scotch, vodka, etc.) drinks per week
---	---	---	---

IF FEMALE EMPLOYEE, GO TO REPRODUCTIVE SECTION, PAGE 25  
IF MALE EMPLOYEE IS MARRIED/DIVORCED/SEPARATED/WIDOWED,  
GO TO SPOUSE SECTION, PAGE 18  
IF NEVER MARRIED MALE GO TO CONSENT FORM

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FEMALE REPRODUCTIVE HISTORY  
(completed by female employees  
and spouses of male employees)

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PAGE 25

Now I would like to ask you questions about your past pregnancies and reproductive history. . .

How many times have you been pregnant, including pregnancies that miscarried, were aborted, or resulted in still-birth or livebirth? Fill in pregnancy history chart for the total number of pregnancies.

\_\_ (if zero, skip to page 35)

**\*\* Pregnancy History Chart \*\***

IF NO PREGNANCIES-SKIP TO PAGE 35	Pregnancy 1	Pregnancy
In what month and year did you become pregnant for the (first/second/third,etc.) time?	__/__ mo yr	__/__ mo yr
Were you under a physician's care during this pregnancy?	-	-
How long were you pregnant?	__ weeks	__ wee
Did this pregnancy result in an abortion, a miscarriage, a stillbirth or a livebirth?	-	-
1=Abortion 2=Miscarriage 3=Stillbirth 4=Livebirth		
Was this a single birth? 0=No 1=Yes	-	-
If no, how many babies were there? (use a separate column for each child)	__	__

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Pregnancy 3	Pregnancy 4	Pregnancy 5	Pregnancy 6
___/___ mo yr	___/___ mo yr	___/___ mo yr	___/___ mo yr
___ weeks	___ weeks	___ weeks	___ weeks
___	___	___	___
___	___	___	___

IF ANY LIVEBIRTHS, CONTINUE TO NEXT PAGE  
 --OTHERWISE IF ABORTION, MISCARRIAGE OR STILLBIRTH CHOSEN  
 SKIP TO PAGE 31

PAGE 27  
 ASK ONLY FOR  
 LIVEBIRTH PREGNANCIES

	Child 1	Child 2
Ask the following for each pregnancy		
What was the date of birth of your first/second, etc. child?	___/___/___	___/___/___
What was the sex of the baby?	-	-
Was this baby premature? 0=No 1=Yes 2=Unsure	-	-
If yes: How premature was this baby?	___ weeks	___ weeks
How much did the baby weigh?	___ lbs ___ oz	___ lbs ___ oz
	(or ___ gms)	(or ___ gms)
How many inches long was the baby?	___ in	___ in
Was labor during this pregnancy natural or induced? (1=natural 2=induced)	-	-
How long did labor last?	___ hrs	___ hrs
Were you given anesthesia during delivery? 0=No 1=Yes 2=Unsure	-	-
If yes, what kind? The choices are- 1=local 2=pudendal 3=spinal 4=epidural 5=general 6=other	-	-
Did you have cesarean delivery? 0=No 1=Yes 2=Unsure	-	-
Was it a breech delivery? 0=No 1=Yes 2=Unsure	-	-
How old is this child currently?	___	___
If died: How old was the child when he/she died?	___ months	___ months
** What was the child's cause of death?	-----	-----
Was an autopsy performed? 0=No 1=Yes 2=Unsure	-	-

Child 3	Child 4	Child 5	Child 6
___/___/___	___/___/___	___/___/___	___/___/___
-	-	-	-
-	-	-	-
___ weeks	___ weeks	___ weeks	___ weeks
___ lbs ___ oz			
(or ___ gms)	(or ___ gms)	(or ___ gms)	(or ___ gms)
___ in	___ in	___ in	___ in
-	-	-	-
___ hrs	___ hrs	___ hrs	___ hrs
-	-	-	-
-	-	-	-
___ months	___ months	___ months	___ months
-----	-----	-----	-----
-----	-----	-----	-----
-	-	-	-

IF ANY CHILD SURVIVED TO ITS 1st BIRTHDAY, CONTINUE TO PAGE 29  
--OTHERWISE SKIP TO PAGE 31









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PAGE 33

Now I would like to ask you about certain dietary and smoking habits during your pregnancies. . .

	Pregnancy 1	Pregnancy 2
Did you consume any coffee, hot or cold tea, soft drinks or other caffeine beverages during any of your pregnancies? 0=No 1=yes 2=Unsure	-	-
If yes: On an average day, how many total cups of coffee, tea, soft drinks or other caffeine beverages did you consume?	__ cups	__ cups
During which months of your pregnancy did you consume these? (write in each month #)		
Did you consume any alcoholic beverage during any of your pregnancies? 0=No 1=yes 2=Unsure	-	-
If yes: Did you consume wine? How many glasses per week?	__	__
Did you consume beer? How many bottles or cans per week?	__	__
Did you consume distilled liquor such as bourbon, gin scotch or vodka? How many drinks per week?	__	__
During which months of your pregnancy did you consume these? (write in each month #)		
Did you smoke during any of your pregnancies? 0=No 1=yes 2=Unsure	-	-
If yes: In total, how many months did you smoke?	__	__
During the time you smoked, on average, how many packs of cigarettes per day?	__	__
During which months of your pregnancy did you smoke (write in each month #)		

Pregnancy 3

Pregnancy 4

Pregnancy 5

Pregnancy 6

\_\_\_\_ cups

\_\_\_\_ cups

\_\_\_\_ cups

\_\_\_\_ cups

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Have you ever used oral contraceptives?  0=No 1=Yes 2=Unsu

If yes, what year did you start using them? 19\_\_

In total, how many years did you use them? \_\_\_ years

Do you know the names of them?  0=No 1=Yes 2=Unsu

If yes, what were they? \_\_\_\_\_

\_\_\_\_\_

Have you ever used contraceptive creams, foams, or jelly with or without a diaphragm?  0=No 1=Yes 2=Unsu

If yes: Did you use any around the time that you conceived any of your pregnancies?  0=No 1=Yes 2=Unsu

If yes: Which pregnancies?  1  2  3  4  5  6

On average, how regularly do/did you have your period. . . was it every month without fail, almost every month or sporadically?  1=Every month wi  
2=Almost every m  
3= Sporadically

On average, how many days is your menstrual cycle? \_\_\_

Did you ever see a doctor for menstrual problems or irregularities?  0=No 1=Yes 2=Unsu

Have your menstrual periods totally stopped?  0=No 1=Yes 2=Unsu

If yes, Did they stop naturally or because of surgery?  1=Naturally  
2=Surgical

How old were you when they stopped? \_\_\_

Have you ever tried for a year or more to become pregnant but were unable?  0=No 1=Yes 2=Unsu

If yes: Could you give me the dates when this occurred . . . from \_\_\_/\_\_\_ to \_\_\_/\_\_\_  
mo yr mo yr

from \_\_\_/\_\_\_ to \_\_\_/\_\_\_  
mo yr mo yr

Have you ever had surgical sterilization?  0=No 1=Yes 2=Unsu

Have you ever been prescribed hormones, such as estrogen, by a doctor for any reason?  0=No 1=Yes 2=Unsu

\*\* If yes: Can you tell me the name of the drug? \_\_\_\_\_

Can you tell me the reason the drug was prescribed?

Have you ever had surgery of the reproductive system?

0=No 1=Yes 2=Unknown

If yes, what kind(s) of surgery?

IF TELEPHONE INTERVIEW OF WIFE, SKIP TO ENDING

IF FEMALE EMPLOYEE WITH PREVIOUS OR CURRENT HUSBAND, CONTINUE BELOW

Now I would like to ask you some questions about your husband's employment history, general health, and diet. First I would like to ask you some background questions. . .

What is your husband's date of birth? \_\_\_/\_\_\_/\_\_\_

What was the highest grade of school your husband completed? \_\_\_

<u>Grade school</u>								<u>High School</u>				<u>College or Vocational</u>				<u>Professional or Graduate School</u>				
1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	1	2	3	4	+
								(13,14,15,16)				(17,18,19,20)								

Could you tell me the job titles your husband has held and for about how long he worked at these jobs?

job title	from	to
-----	___/___ mo yr	___/___ mo yr
-----	___/___ mo yr	___/___ mo yr
-----	___/___ mo yr	___/___ mo yr
-----	___/___ mo yr	___/___ mo yr

Could you tell me any chronic health problems your husband has had during the past five years? These may include diabetes, hypertension or others.

-----  
-----

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Could you tell me about any serious acute health problems or conditions requiring surgery, your husband has had during the last five years?

-----  
-----

Has your husband ever smoked at least 1 cigarette a day for as much as 3 months?      0=No 1=Yes

GO TO CONSENT FORM

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MALE EMPLOYEE WITH PREVIOUS OR CURRENT SPOUSE

Now I would like to ask you some questions about your wife's employment history, general health, diet and pregnancy history. Many of these questions are similar to those I have already asked of you.

Could you tell me the job titles your wife has held and for about how long she has worked at these jobs?

job title	from	to
-----	___/___ mo yr	___/___ mo yr
-----		___/___ mo yr
REPRODUCTIVE HISTORY (completed by male employees)		___/___ mo yr
-----	___/___ mo yr	___/___ mo yr

Could you tell me any chronic health problems your wife has had during the past five years? These may include diabetes, hypertension, or others.

-----

-----

Could you tell me about any serious acute problems or conditions requiring surgery, your wife has had during the last five years?

-----

-----

Does your wife now, or did she ever, drink coffee, tea or soft drinks containing caffeine on a regular basis?

0=No 1=Yes 2=Unsure

If yes: Which? . . .

Caffeinated Coffee	Caffeinated Hot tea	Caffeinated Cold tea	Soft drinks containing caffeine
-----	-----	-----	-----
--	--	--	--

Has your wife ever smoked at least 1 cigarette a day for as much as 3 months? 0=No 1=Yes 2=Unsure

Now I would like to ask you questions about your wife's past pregnancies and reproductive history. . .

How many times has your wife been pregnant, including pregnancies that miscarried, were aborted, or resulted in stillbirth or livebirth? Fill in pregnancy history chart for the total number of pregnancies.

-- (if zero, skip to consent form)

**\*\* Pregnancy History Chart \*\***

IF NO PREGNANCIES--SKIP TO CONSENT FORM	Pregnancy 1	Pregnancy 2
Did this pregnancy (these pregnancies) result in an abortion, a miscarriage, a stillbirth or a livebirth?	-	-
1=Abortion 2=Miscarriage 3=Stillbirth 4=Livebirth		
Was this a single birth? 0=No 1=Yes	-	-
If no, how many babies were there? (use a separate column for each child)	--	--
In what month and year did this occur?	__/____ mo yr	__/____ mo yr
What is the age of this child currently?	--	--
If died: How old was the child when he or she died?	-----	-----
**What was the child's cause of death?	-----	-----
Was an autopsy performed? 0=No 1=Yes 2=Unsure	-	-
If livebirth: What was the sex of this child? 1=Male 2=Female 3=Unsure	-	-

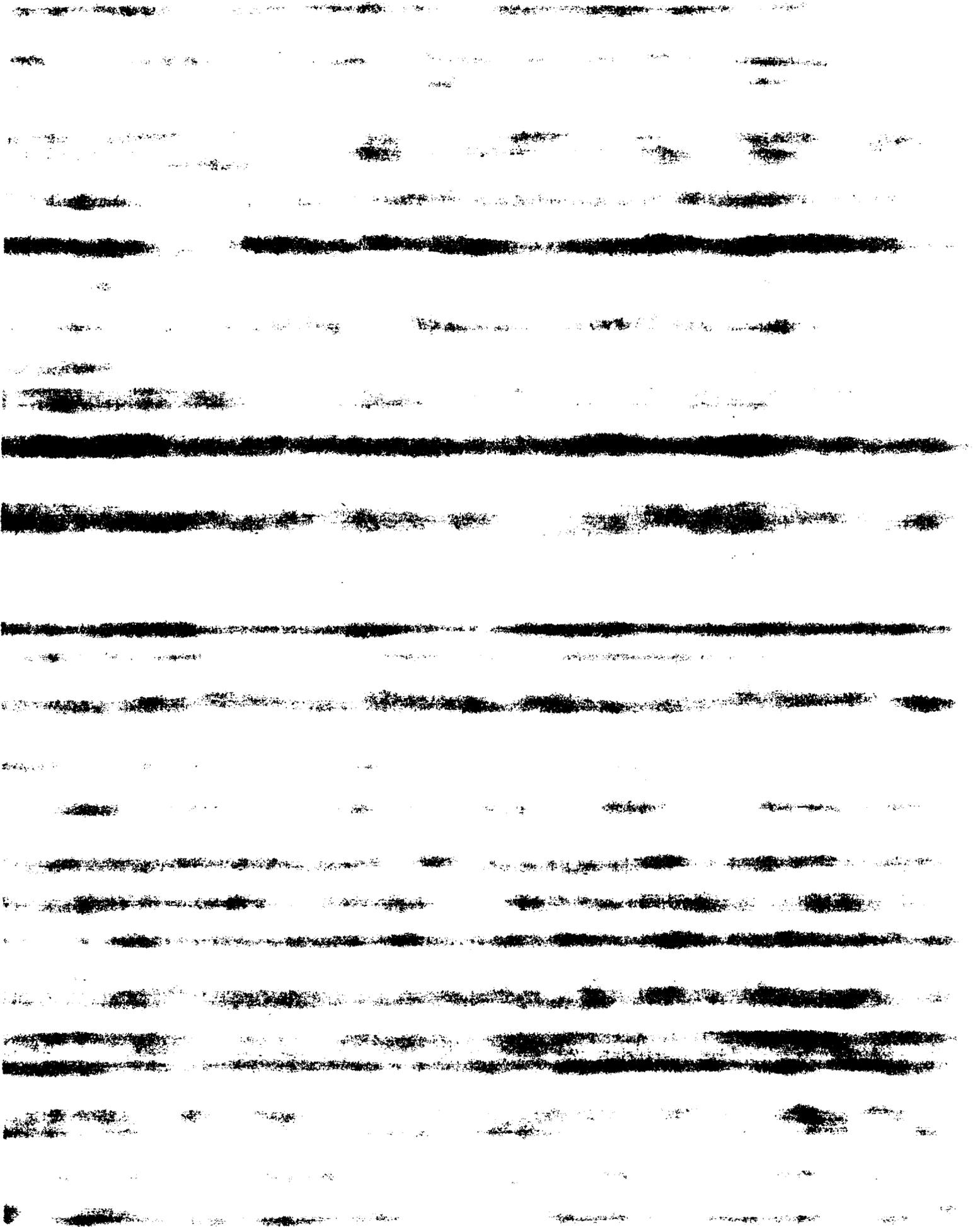
Pregnancy 3	Pregnancy 4	Pregnancy 5	Pregnancy 6
-	-	-	-
-	-	-	-
-	-	-	-
mo yr	mo yr	mo yr	mo yr
-	-	-	-
-	-	-	-
-	-	-	-
-	-	-	-
-	-	-	-
-	-	-	-
-	-	-	-
-	-	-	-
-	-	-	-
-	-	-	-











Questionnaire

Section I

Could you tell me the job titles which you have held before working at Digital in Hudson and when you worked at these jobs?

<u>Job Title</u>	<u>From</u>	<u>To</u>
_____	mo. / yr.	mo. / yr.
_____	mo. / yr.	mo. / yr.
_____	mo. / yr.	mo. / yr.
_____	mo. / yr.	mo. / yr.

Section II

During the past 5 years, have you had any of the following medical conditions?

Diabetes? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: How long have you had diabetes? \_\_\_\_\_ years

High Blood Pressure? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: How long have you had high blood pressure? \_\_\_\_\_ years

During which years did you have high blood pressure? Circle all that apply.

1982    1983    1984    1985    1986

What medications have you taken for this? \_\_\_\_\_  
\_\_\_\_\_

Cancer? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: What type of cancer did you have? \_\_\_\_\_

When was your cancer first diagnosed? \_\_\_\_\_  
mo. / yr.

\*\*Did you receive any radiation treatment or chemotherapy?

\_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

Thyroid Problems? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes:\*\*Is it an over-active thyroid problem or an under-active one?

\_\_\_\_\_ 1 = over-active 2 = under-active

During which years did you have a thyroid problem? Circle all that apply.

1982 1983 1984 1985 1986

Gallbladder Problems? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: During which years did you have a gallbladder problem? Circle all that apply.

1982 1983 1984 1985 1986

Respiratory Problems such as asthma, chronic bronchitis or pneumonia? \_\_\_\_\_  
0 = no, 1 = yes, 2 = unsure

If yes: Did you have asthma? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

During which years did you have asthma? Circle all that apply.

1982 1983 1984 1985 1986

Did you have chronic bronchitis? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

During which years did you have chronic bronchitis? Circle all that apply.

1982 1983 1984 1985 1986

Did you have pneumonia? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

During which years did you have pneumonia? Circle all that apply.

1982 1983 1984 1985 1986

Kidney Disorders? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: How long have you had a kidney disorder? \_\_\_\_\_ years

Convulsive Disorders? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: During which years did you have a convulsive disorder.  
Circle all that apply.

1982 1983 1984 1985 1986

In total, how many months did this condition last? \_\_\_\_\_

Arthritis? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: How long have you had arthritis? \_\_\_\_\_ years

Anemia or Low Blood Count? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: How long were you anemic? \_\_\_\_\_ years

During which years were you anemic? Circle all that apply.

1982 1983 1984 1985 1986

In total, how many months did this condition last? \_\_\_\_\_

Slipped Disc? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: What year did you have a slipped disc? 19 \_\_\_\_\_

How was it diagnosed (x-rays, CAT scan, etc.)? \_\_\_\_\_

Other Back Problems? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: What kind of problem do/did you have? \_\_\_\_\_

How long have you had this back problem? \_\_\_\_\_ years

Frequent or Severe Sore Throats? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure  
(frequent means more than 2 per month)

If yes: Were they frequent, severe or both? \_\_\_\_\_ 1 = frequent, 2 = severe, 3 = both

During which years did you have these sore throats? Circle all that apply.

1982 1983 1984 1985 1986

In total, how many months did this condition last? \_\_\_\_\_

On average, how many times per month did you have these sore throats? \_\_\_\_\_

Frequent or Severe Headaches? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure  
(frequent means more than 3 per month)

If yes: Were they frequent, severe or both? \_\_\_\_\_ 1 = frequent, 2 = severe, 3 = both

During which years did you have these headaches? Circle all that apply.

1982 1983 1984 1985 1986

In total, how many months did this condition last? \_\_\_\_\_

On average, how many times per month did you have these headaches? \_\_\_\_\_

Frequent or Severe Rashes? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure  
(frequent means more than 2 per month)

If yes: Were they frequent, severe or both? \_\_\_\_\_ 1 = frequent, 2 = severe, 3 = both

During which years did you have these rashes? Circle all that apply.

1982 1983 1984 1985 1986

In total, how many months did this condition last? \_\_\_\_\_

On average, how many times per month did you have these rashes? \_\_\_\_\_

Frequent or Severe Dizziness? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: Were they frequent, severe or both? \_\_\_\_\_ 1 = frequent, 2 = severe, 3 = both

During which years did you have dizziness? Circle all that apply.

1982 1983 1984 1985 1986

In total, how many months did this condition last? \_\_\_\_\_

On average, how many times per month did you have dizziness? \_\_\_\_\_

Frequent or Severe Eyestrain? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: Was this frequent, severe or both? \_\_\_\_\_ 1 = frequent, 2 = severe, 3 = both

During which years did you have eyestrain? Circle all that apply.

1982 1983 1984 1985 1986

In total, how many months did this condition last? \_\_\_\_\_

On average, how many times per month did you have eyestrain?  
\_\_\_\_\_

Frequent or Severe Nausea? \_\_\_\_\_ 0 = no, 1 = yes, 2 = unsure

If yes: Was this frequent, severe or both? \_\_\_\_\_ 1 = frequent, 2 = severe, 3 = both

During which years did you have nausea? Circle all that apply.

1982 1983 1984 1985 1986

In total, how many months did this condition last? \_\_\_\_\_

On average, how many times per months did you feel nauseous?  
\_\_\_\_\_

### Section III

Do you use sugar substitutes, such as saccharin or nutrasweet? \_\_\_\_\_  
0 = no, 1 = yes, 2 = unsure

If yes: How many teaspoons per week of saccharin do you use? \_\_\_\_\_

How long have you been using saccharin? \_\_\_\_\_

How many teaspoons per week of nutrasweet do you use? \_\_\_\_\_

How long have you been using nutrasweet? \_\_\_\_\_

### Section IV

Have you ever smoked at least one cigarette a day for a long as three months? \_\_\_\_\_  
0 = no, 1 = yes, 2 = unsure

Have you ever smoked pipes or cigars for as long as three months? \_\_\_\_\_  
0 = no, 1 = yes, 2 = unsure

If yes to either of the last two questions:

	<u>Cigarettes</u>	<u>Pipes or Cigars</u>
At what age did you begin smoking?	_____	_____
In total, for how many years have you smoked?	_____	_____
Are you a current smoker?	0 = no, 1 = yes, 2 = unsure	
Have you been a regular smoker during the past five years?	0 = no, 1 = yes, 2 = unsure	

If no to the above: In which of the past five years were you a smoker? Circle all that apply.

1982 1983 1984 1985 1986

On average, how many packs per day have you smoked during the past five years? \_\_\_\_\_

Do you smoke more, less or about the same as ten years ago?  
\_\_\_\_\_ 1 = more, 2 = less, 3 = same

Do/did you usually smoke low-tar cigarettes, regular filtered cigarettes, unfiltered cigarettes, pipes or cigars? Circle all that apply.

low-tar cigarettes

regular filtered cigarettes

unfiltered cigarettes

cigars

pipes

When you smoke/smoked, do/did you usually inhale into the chest, into the throat or not inhale at all? \_\_\_\_\_

1 = chest, 2 = throat, 3 = not at all

Have you ever used snuff or chewing tobacco? \_\_\_\_\_  
0 = no, 1 = yes, 2 = unsure

If yes:

	<u>Snuff</u>	<u>Chewing Tobacco</u>
At what age did you use snuff and/or chewing tobacco?	_____	_____
In total, for how many years did you use snuff and/or chewing tobacco?	_____	_____
On average, how many times per week did you use snuff and/or chewing tobacco?	_____	_____
Are you a current user of snuff and/or chewing tobacco?	_____	_____

0 = no, 1 = yes, 2 = unsure

Section V (Only if spouse of male employee)

Could you tell me any chronic health problems which you have had during the past five years? These may include diabetes, hypertension or others.

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Could you tell me about any serious acute problems or conditions requiring surgery which you have had during the past five years?

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